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Advancing our understanding of major depression and its assessment using experience sampling methodology

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Declaration

I hereby declare that this thesis is my own composition and that the work reported here has been carried out by myself (except where due acknowledgement is made in the text). This work has not been submitted for any other degree or professional qualification.

Yu-Mei Li

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Abstract

The development of the classification systems of psychiatric disorders illustrates a long-term debate on whether a discrete and categorical or a continuum and spectral view best describes psychiatric disorders. This is because comorbidity between mental disorders is common and the symptoms of the same psychiatric disorders are heterogeneous. These all increase the difficulty to diagnose and to treat mental disorders. Generally, the diagnostic systems have attempted to develop diagnostic criteria of psychiatric disorders that resemble a solid medical model, where each disorder is described by a discrete category of symptoms. However, these attempts have been plagued by problems. Even though having a categorical classification system makes diagnoses easier than having nothing to work from, a categorical classification system cannot *explain* clinical conditions. Having alternative classification systems such as one based on dimensions (spectra) or a mixture of categorical and spectral classification systems may be better than using either classification system alone. It has been suggested that a mechanistic property clusters (MPC) would be a suitable alternative (Kendler et al., 2011). The MPC described psychiatric disorders are caused by multi-level causal loops and interactions. A similar view of symptoms forming a causal network – the network theory – has been advocated (Borsboom, 2008, 2017). The network theory hypothesizes that the present psychiatric symptoms are caused by the same and/or other psychiatric symptoms occurred earlier.

This PhD project investigated the heterogeneous nature of the symptoms of major depression (MD) by using their repeated measures in daily-life settings in three studies. We used on-line questionnaires, mobile questionnaires, and activity sensors. MD symptoms at the moment were measured using mobile questionnaires and daily physiological signals were recorded using activity sensors. The on-line questionnaires were administered before and after the participants completed the momentary questionnaires. Study 1 measured the momentary MD symptoms using

Android devices, Study 2 was a replicate of Study 1 and iOS devices were employed in Study 2. Study 3 measured the momentary MD symptoms and activity levels using Android and iOS devices and activity sensors. Study 3 was a replication of Studies 1 and 2. The replicability of the results across the three studies was tested. Meta-analysis was used to see whether there were similar patterns across studies. In addition to the network theory, discriminant and convergent validity of the mobile and retrospective MD assessments were tested. The heterogeneity of MD symptoms was examined in the relationships between momentary MD symptom ratings and controlling factors (i.e., age, gender, employment status, marital status, educational level, MD severity, circadian rhythm, personality traits and facets, daily activity and heart rate variability). The results suggested heterogeneity among MD symptoms in how they linked to other variables. These findings challenge the existing clinical practice of using the total sum-score of symptoms in clinical diagnoses. Marginal support for the network theory was reported. The findings showed moderate replicability across studies.

Lay summary

Mental disorders are hidden disorders. Unlike some physical diseases that have apparent symptoms such as coughing, sneezing, or fevers, people with mental disorders usually do not show easily observable symptoms and the symptoms used to diagnose a mental disorder are fairly different. Despite the symptoms used to diagnose a single mental disorder being diverse, the diagnoses of mental disorders primarily rely on a single number – sum-total score of symptoms. This thesis explored the differences in the symptoms of a mental disorder – major depression (MD). In three studies, mobile questionnaires presented on applications in both Android and iOS devices were used to collect changes in MD symptoms 4–6 times per day for 14–15 days. On-line questionnaires were used to collect the demographics and baseline information. In one of the three studies, an additional device, activity sensors, were used to gather information on activity level and heart rate variability. The relationships between MD symptoms and the following were examined: moderators including age, gender, educational attainment, marital status, and employment status, MD severity, circadian rhythm, personality, activity level, and heart rate variability. One possible explanation for the causes of MD – whether the symptoms form an inter-connected network and exhibit time-varying causal relationship – was investigated, too. The results revealed variability among individual MD symptoms and suggested revising the diagnostic criteria currently in-use. Limited evidences for causal relationships between MD symptoms were found.

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Chapter 1 Literature review

"Classification is usually said to serve one or more of three interconnected aims: (1) to help us understand, order, and communicate information; (2) to establish jurisdiction or boundaries – for example, between human beings and animals, what is edible and not edible, what is therapeutic and noxious; and (3) to establish legitimacy and thus facilitate control of the environment, animate as well as inanimate. …" (Szasz, 1997, p. 11)

This chapter begins with the history of two classification systems of psychiatric disorders, followed by the diagnostic criteria of major depression (MD), heterogeneity of MD, the research method used in this thesis, and ended with a brief introduction of the following chapters.

The history of the development of the classification systems of psychiatric disorders unveils the changes in the mainstream theories in psychiatry. There are two widely used classification systems – the Diagnostic and Statistical Manual (DSM) and the International Classification of the Disease (ICD). Both classification systems pooled symptoms together to establish diagnoses of mental disorders. However, diverse symptom profiles have been observed in patients. It implies heterogeneity in MD symptoms and challenges the categorizations of mental disorders. It also brought about the first research question in this thesis – are MD symptoms homogeneous or heterogeneous? This question was tested by using measures of MD symptoms and variables including MD severity, demographics, circadian rhythm, personality traits and facets, activity level, and heart rate variability (Chapters 2–6).

The other research question touched upon possible explanations of MD. One popular explanation is essentialist view (Kendler et al., 2011). It describes symptoms of a disease or disorders are caused by one underlying cause. A good example well-explained by essentialist view is infectious diseases, where patients recover from their illnesses after the elimination of the targeted bacteria. Even

though the two classification systems do not address the underlying causes of mental disorders, grouping different symptoms together and giving them equal weights (except the main symptoms) may imply a hidden assumption that the depressive symptoms are caused by one underlying cause (essentialist view or latent variable theory). However, diverse disorder profiles observed in depression patients and comorbidity between depression and other psychiatric disorders may suggest there are other explanations. The latent variable theory nicely explains infectious diseases but it might not be a satisfying explanation for mental disorders.

Another theory that looks at the causal relationships among symptoms provides an alternative insight into depression. This theory is termed network theory. In my thesis, the network theory was tested by using time-series data from 277 participants in three different studies and a meta-analysis of the three studies. The data were analyzed using temporal, contemporaneous, and between-subject networks to examine the numbers of significant associations in temporal networks and the topography of depressive symptoms in the three types of networks (Chapter 7).

Classification system in psychiatry

The study of the epidemics of mental disorders firstly began with studying the patients in asylums in the 19th century (Demazeux, 2014). There was no classification system to guide diagnoses until 1949 (Rössler, 2013). The early psychiatrists were not interested in having a classification system even though there was a need in diagnoses. They were more interested in applying classification systems in asylum management (Grob, 1991). Two main classification systems are used by psychiatrists – the ICD of the World Health Organization and the DSM of the American Psychiatric Association (APA). A section detailing psychiatric disorders was firstly included in the ICD in 1949 (Rössler, 2013; World Health Organization, 2006). Later in 1952, the first edition of the DSM was published (American Psychiatric Association, 2018). The ICD was developed by an international organization to be used by the member countries of the World Health Organization (WHO) while the

DSM was developed and mainly used by the psychiatrists in the U.S. (American Psychological Association, 2009; Jablensky, 2009). The WHO widely distributed the ICD at a low cost, but the DSM continued to generate huge revenue for the APA.

Classification systems provide a common ground for clinicians and researchers to diagnose cases and conduct research. These classification systems are not flawless and several revisions and editions of the ICD and the DSM have been published after the release of the first editions of the two classification systems.

The development of classification system is "shaped by a variety of factors: the social origins and ideological, political, and moral commitments of psychiatrists; their desire for status and legitimacy; the characteristics of their patients; the nature and location of their practices; and the broader social and intellectual currents prevalent at a given time" (Grob, 1991, p. 421). Looking at the brief history of the development of psychiatric classification system may help us to see how psychiatry becomes what it is today and the rises and falls of different theories. However, historical recollections are not without biases and potential flaws. The limitations of historical recollection are – "by the very selection of key historical phenomena deemed to be worthy of inclusion in any account, and by the different emphasis on, and chronological linkages between diverse components of such an account, the final product is often far from being wholly 'objective' and/or comprehensive" (Kawa & Giordano, 2012, p. 2).

The pushes from outside of psychiatry – social sciences, federal census, and the statistics and epidemiology of psychiatric disorders – urged the compiling of the first edition of the DSM (Demazeux, 2014; Grob, 1991). Through studying the mental health condition of some communities in Chicago, several sociologists applied their research in medicine. Psychologists contributed in designing standardized tools, instruments and statistical methods, which shaped psychiatry and the structure of the psychiatric classification system. The federal census' main concern was to apply the classification system in policy. Many thought "statistical

knowledge could thus serve as the foundation for social policy and end the pernicious bickering over theory, principles, and politics" (Grob, 1991, p. 424).

During the development of classification systems, there were times when the biological causes were favored and there were other times when the societal-environmental causes were the mainstream. However, these two causes are not mutually exclusive, and they may both influence the formation of psychiatric disorders from different angles. Psychiatrists considered mental disorders were caused by both psychosocial and biological factors but they thought these two factors related inversely (Ahn et al., 2009). For example, if a psychiatric disorder was to have a strong root in biology, clinicians would regard psychosocial factors as only having a small influence on the disorder. Ahn et al. (2009) also found that psychiatrists gestated some mental disorders to have stronger roots in biology and others to have more psychosocial origins. They deemed biological-based psychiatric disorders would be better treated by using medications than other treatments and psychotherapy would be a more appropriate treatment for psychosocial-based psychiatric disorders. Psychologists and social workers were found to have similar thoughts to psychiatrists.

The development of the DSM

The competition between the biomedical model and biopsychosocial model could be observed in the revisions of the DSM (Braslow, 2000). Before the DSM-I was published, psychodynamic theories dominated the field of psychiatry (Kawa & Giordano, 2012). As the influences of environmental stressors gradually gained a broad recognition, the concept of psychopathology shifted from discrete categories to a continuum of severity. The scope of the DSM-I was relatively narrow and it only covered organic and psychotic disorders (Blashfield et al., 2014). The next edition – the DSM-II – was released in 1968 to solve the problems found in the DSM-I. The DSM-II remained greatly influenced by psychodynamic theories (Kawa & Giordano, 2012). In the 1960s, the attackers of psychiatry – anti-psychiatrists – argued because there had not been a clear boundary between the definitions of mentally ill and mentally healthy, the diagnoses of psychiatric disorders may not be trustworthy

(Wilson, 1993). Among those, Rosenhan (1973) reported researchers pretended to be psychiatric patients (pseudopatients) and some psychiatrists could not tell their disguises and they were later admitted into psychiatric hospitals. This article greatly challenged the field of psychiatry and put psychiatry in a trust crisis. In addition, his study spurred discussions on whether the diagnoses of psychiatric disorders were legitimate. Even decades later, there were replications (Slater, 2005) and discussions (Spitzer et al., 2005; Zimmerman, 2005) of his study. Other criticisms included social control of labelling and psychiatric disorders did not exist. While Rosenhan (1973) told a compelling story and threatened the existence of psychiatry as a discipline, there were criticisms of the experiment design and the interpretation of the results (Ruscio, 2004; Spitzer et al., 2005). In Cahalan's (2020) book, she delved into every identifiable trace she could find to put together the details of the Rosenhan experiment. Through several sources including interviews, Rosenhan's archives, medical records and a commentary (Cahalan, 2017), she revealed questionable interpretations and even fabrications of the pseudopatients' experiences in those hospitals. Cahalan cannot be certain whether Rosenhan had misconducted but her book did raised doubts toward Rosenhan's (1973) experiment. Researchers and policy makers should be more cautious when applying the results in the future. If Rosenhan's experiment was included in textbooks, the authors could consider to cover the relevant criticisms to train critical thing skills in students (Bartels & Peters, 2017).

Moreover, services provided by other health professionals within psychiatry also caused psychiatrists wanting to distinguish themselves from other health providers within psychiatry (Mayes & Horwitz, 2005). These are the historical backgrounds surrounding the development of the DSM-III. To address the problems and coincident the fall of psychoanalysis and the rise of psychopharmacology, the DSM-III was published in 1980. It adopted a biopsychosocial model (Ghaemi, 2009) and aimed to standardize the diagnostic criteria (Demazeux, 2014).

Different from the previous editions where the definitions were short, general, and broad, the diagnostic criteria in the DSM-III were clearly defined by

lengthy explanations, which created categories of mental disorders (Blashfield et al., 2014). The drastic changes in the DSM-III from psychodynamics (as best represented by Emil Kraepelin), were called neo-Kraepelinian (Compton & Guze, 1995). These detailed descriptions worked well in setting up boundaries between psychiatric disorders and as a result, making it easier for psychiatrists to prescribe medications and for patients to apply for insurance compensations (Blashfield et al., 2014). The DSM-III greatly influenced both the clinicians and researchers. It was widely adopted in psychiatric training and in academic publishing and by psychiatrists in practice. It also boosted psychopharmacological research projects funded by the U.S. government and pharmaceutical companies (Gambardella, 1995). Stringent diagnostic criteria greatly raised the reliability of diagnoses compared to the previous two editions of the DSM.

But despite the improvements, the DSM-III was not problem-free. It still received lots of criticisms and the behind-the-scene story of how the DSM-III was developed revealed the decisions were made based on consensus of a small group of like-minded psychiatrists (Davies, 2017). The increases in prescribing psychiatric medications had raised some issues in several mental disorders including MD, where in some cases antidepressants were not used to cure or improve a medical condition in patients but to enhance mood in normal people (Kramer & Brody, 1994). Other issues were simplifying social and familial problems by mass drug prescriptions to children diagnosed with attention-deficit/hyperactivity disorder (ADHD), diagnosing those who had symptoms of shyness as having social anxiety disorder, and people with less severe symptoms of post-traumatic stress disorder received the diagnoses because of compensation claim applications (Bracken & Petty, 1998).

A revision of the DSM-III, the DSM-III-R, was published in 1987 to correct the considerable mistakes in the diagnostic criteria in the DSM-III according to relevant empirical data (Blashfield et al., 2014). Some clinicians argued the DSM-III-R was essentially the DSM-IV rather than merely a revision (Zimmerman, 1988). The critics of the DSM-III-R such as Wakefield (1992, 1999) argued that the definition of

disorder in the DSM-III-R implied disorders were harmful and dysfunctional. Since both harmful and dysfunctional were based on value judgment and changing societal and personal values reflect changes in value judgement, using harmful and dysfunctional to define psychiatric disorders may affect how the disorders were viewed and diagnosed. This entailed the classification system may require periodical updates depending on changes in societal and personal values and there may never be a finalized edition (Blashfield et al., 2014).

In 1988, less than one year after the publication of the DSM-III-R, the APA announced the preparation of the DSM-IV will start. The DSM-IV was published in 1994, two years after its' scheduled year of publication. The frequent revision of the diagnostic criteria drew the attentions of some clinicians. They felt confused with the changes and criticized the frequent revision of the diagnostic criteria had left them with limited amount of time to stabilize their diagnoses (Zimmerman, 1988).

Clinical significance – whether the severity of symptoms resulted in significant distress or impairment in daily functioning – was included in the DSM-IV. This was used to reduce the rate of false diagnosis. The DSM-IV-TR, a text revision of the DSM-IV, contained some minor revisions was published in 2000 (Blashfield et al., 2014). Thirteen years later, the DSM-V was published in 2013. The number of psychiatric diagnostic criteria increased with the publication of the new editions and revisions of the DSM (Figure 1.1). Starting from the DSM-III, the shift from a continuum of symptom severity to discrete categories could be found in later editions or revisions of the DSM despite some broader definitions were included in the DSM-V – "an implicit flexible definition of mental disorder, including dimensional models for some disorders and retaining fuzzy prototypes for others" (Blashfield et al., 2014, p. 38). Rössler (2013) suggested returning to the broad and general continuum definition of diagnostic criteria may be the way forward. This is because many people who have sub-clinical disorders have functional disability, too. Also, by adopting the continuum definitions, the constant and normal fluctuations of psychiatric symptoms could be appropriately addressed. The possible disadvantages of the continuum definitions or the dimensional models were the

number of symptoms or dimensions required in clinical diagnoses, missing matric in determining severity, and the applications in daily clinical practice were not as straightforward as the categorical models (Jablensky, 2009). Since both the categorical and the dimensional models have their advantages and disadvantages and they were not mutually exclusive, adopting both models in classification systems may be a more promising solution than using either one of the two models alone.

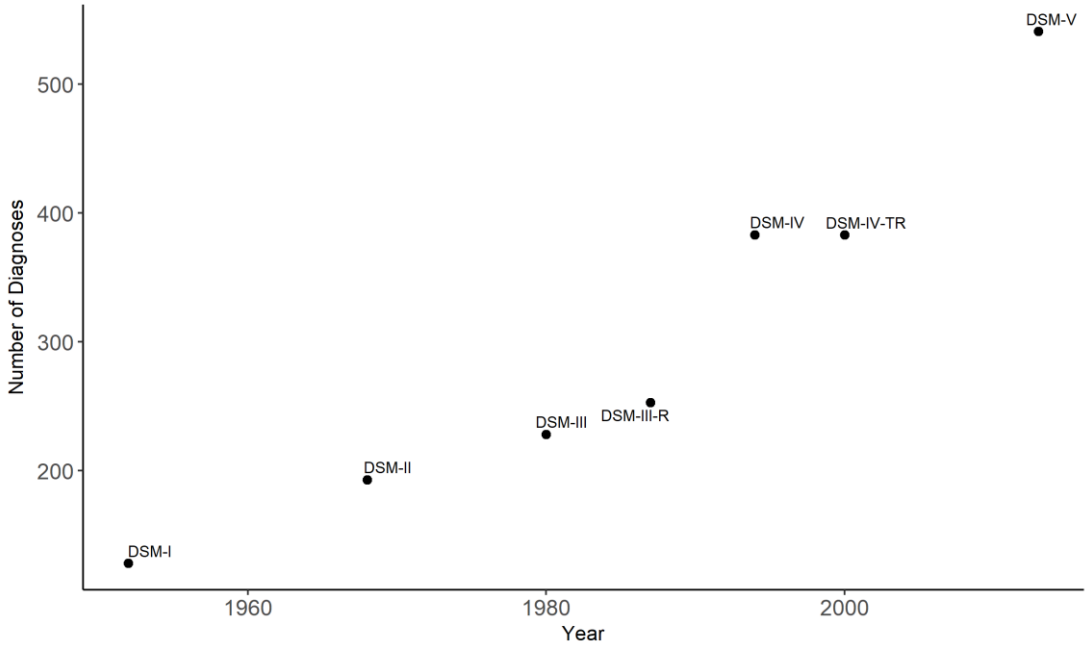


Figure 1.1 *Year of publication and numbers of categories in different versions and revisions of the DSM*

The ICD vs. the DSM

The publication of the DSM-I also revealed the existences of enormous disparities between the ICD-6 and the DSM-I (Blashfield et al., 2014). Later, the WHO assembled international committees in different countries around the world to establish a classification system. The resulting ICD-8 was nearly identical to the DSM-II. But the next version of the DSM-II, the DSM-III was quite different from the ICD-8 due to very few international participation in preparing for this edition of the DSM (American Psychological Association, 2009). In the next version of ICD, the ICD-

9, no diagnostic criteria were included and it was very different from the DSM-III (American Psychiatric Association, 2018). Because of this, to use the ICD-9 in the U.S., a modification of the ICD-9, the ICD-9-CM, was published later. Even though the DSM-IV and the ICD-10 were developed closely together and they were highly similar, differences in concepts and matters such as ways of operationalizing diagnoses were reported (First, 2009). Among the 176 diagnostic criteria, only one disorder – transient disorder – had the same diagnostic criteria in both classification systems. The latest version of the ICD, ICD-11, was published in June 2018 (World Health Organization, 2018).

It took longer to develop the latest versions of the DSM and the ICD. The gaps between the two latest editions of the DSM and the ICD are more than 20 years – 21 for the DSM and 26 years for the ICD. Both the DSM-V and the ICD-11 do not include the explanations for the underlying causes of mental disorders. But they differ in the use of functional impairments, which are used in the DSM but not in the ICD (Gaebel, 2015). The ICD dominates clinical diagnoses in the U.K. while the DSM is the mainstream classification system of mental disorder diagnoses in the U.S. (Tyrer, 2014). In other countries, clinicians could either choose between the two classification systems or combine them depending on what they consider as useful in their clinical practices.

The National Institutes of Health (NIH) in the U.S. is not satisfied with the DSM-V and funds a project to develop a new classification system to be used for research purposes – the Research Domain Criteria (RDoC) (Insel, 2014; Insel et al., 2010). The NIH also redirects research away from the DSM-V and encourage researchers to go beyond the existing categories to investigate a broader scope of mental disorders (Insel, 2013). Precision medicine – establishing "a diagnostic system based on a deeper understanding of the biological and psychosocial basis of a group of disorders" – for psychiatry was the goal set for the RDoC (Insel, 2014, p. 396). This is carried out by incorporating data from several levels including symptom, society, genetics and neurology. An alternative classification system – the Hierarchical Taxonomy of Psychopathology (HiTOP) model – was proposed by

several psychologists and psychiatrists (Kotov et al., 2017). Closely related symptoms are grouped together to address issues in comorbidity and heterogeneity. Dimensional measures are used to cover a broad range of symptomatic states. The HiTOP model is still in its' early stage and there are a few limitations such as lacking empirical research in some dimensions and in young people and the elderly.

The brief history of psychiatric classification systems, especially the discrepancies between the two main classification systems, competing theories, the developing of new classification systems, and an unsettling problem in comorbidity, which describes the overlapping of symptoms between different psychiatric disorders, tell us that the field is still evolving. Despite classification systems are there to establish a common ground for professionals working within psychiatry to communicate and further the development of the field, thinking diagnostic criteria represent complete profiles of mental disorders in clinical care and research may stop the clinicians and researchers from exploring the characteristics of psychiatric disorders not currently covered in the diagnostic criteria in the DSM or the ICD. This may lengthen the search for other potentially effective treatments. The problem with comorbidity mainly lies in unspecific treatments, where the same medication is used to treat several psychiatric disorders (i.e., serotonin reuptake inhibitors is a commonly prescribed medication for MD, anxiety disorder, and obsessive-compulsive disorder etc.). To see whether individual symptom of a psychiatric disorder, MD, relates similarly or differently to factors influencing MD, this thesis will take a closer look at the relationships between MD symptoms and several factors.

Clinical diagnoses and the classification systems

Even though the DSM dominate the training courses and programs psychiatrists attended, the guidelines the researchers must follow to publish in academic journals, and the research funding applications, little is known regarding how clinicians conceptualize mental disorders and how these resemble the categories of mental disorders listed in the DSM. Research into this would inform how the clinicians use the DSM. It has been reported that clinicians' taxonomies of

mental disorders are different from the DSM (Flanagan & Blashfield, 2007; Kim & Ahn, 2002). Clinicians' taxonomies and the DSM correlate moderately and their taxonomies have a smaller number of diagnostic categories than those in the DSM (Flanagan & Blashfield, 2007). Also, since neither the DSM nor the ICD are based on any theory and do not explain the causal mechanisms underlying psychiatric disorders, clinicians may make clinical decisions based on their own theory-based representations (Kim & Ahn, 2002). Clinicians tend to have better recall of the symptoms that were close to their theories than the symptoms that were further away from their theories.

Biomarkers of psychiatric disorders

The search for biomarkers of psychiatric disorders has been futile due to several reasons (Kapur et al., 2012). First, lacking a gold standard because the classification systems in use are not designed to explain the biological mechanisms. Second, there have been many underpowered studies. Third, the replications are close, but they are not exact replicates of the previous studies. Lastly, comparisons between patients and normal controls are commonly used in study designs, thus making such comparisons legitimate. However, it is uncommon that clinicians would compare mental disorder patients with normal people in clinical settings because these two groups are incomparable. This should be applied in empirical studies, too.

Unable to identify biomarkers of psychiatric disorders may hinder the search for "personalized medicine" or "precision medicine" of psychiatric disorders. Therefore, Kapur and colleagues (2012) suggested replacing "personalized medicine" with a more realistic approach – "stratified medicine", which was proposed by Trusheim, Berndt, and Douglas (2007). In stratified medicine, biomarkers or cognitive tests are used to stratify patients with diagnosed disorders into subgroups to assist the clinicians to prescribe the most suitable treatments. Adopting stratified medicine may be beneficial because of several reasons, which include avoiding the debates on the benchmark, does not require a full understanding of the etiology of psychiatric disorders, and could be readily applied in the classification systems currently in use (Kapur et al., 2012). To find a way out of the deadlock, the NIH

introduced the RDoC to identify biomarkers, behavioral or cognitive symptoms that could be used in stratified medicine.

Major Depression and its diagnostic criteria

MD was reported as a common mental disorder in the National Comorbidity Survey Replication, which was a large national survey conducted in the U.S. in the early 2000s (Kessler, 2003). In another large group of American participants, the prevalence of MD among African Americans and Caribbean blacks was lower than that in non-Hispanic whites (Williams et al., 2007). A cross-cultural study showed the prevalence rate of MD differed from country to country – lifetime prevalence ranged from 1.9% in Taiwan to 19% in Beirut (M. M. Weissman et al., 1996). Another multinational study also reported similar results of varying prevalence between the countries been surveyed – lifetime prevalence ranged from 3% in Japan to 16.9% in the U.S. (Andrade et al., 2003). However, societal and cultural influences on how mental disorders are viewed and conceptualized in different countries may contribute to the disparities between countries.

The impacts of MD are pervasive. Some MD patients had a hard time to fulfil their social roles and various aspects of their social capabilities were affected (Kupferberg et al., 2016). Having MD not only change the way people feel about themselves but also alter how they feel about the surrounding environments (Gotlib & Joormann, 2010). The diagnostic criteria for MD in the DSM-V covered nine symptoms – depressed mood most of the day, loss of interest or pleasure in almost all activities, altered appetite and significant weight loss or gain, psychomotor retardation or agitation, fatigue or loss of energy, feeling worthless or guilt, insomnia or hypersomnia, diminished ability to think, poor concentration, or indecisiveness, and recurring thoughts of death or suicidal ideation (American Psychiatric Association, 2013a). The diagnosis of MD is established when five or more symptoms continuously cause clinical distress in an individual or greatly impair his/her social functioning for more than two weeks. In addition, one out of the five symptoms should be either depressed mood or loss of interest or pleasure.

The life-time recurrence rate of MD is approximately 40% and ranges from 17% to 76% (Mattisson et al., 2007). This indicates that on average, 60% of the MD patients only have one MD episode in their lifetime. The results from 12 cohorts reported the recurrence rates of MD ranged from 7% to 65% (Steinert et al., 2014). People who stayed in specialized mental healthcare settings had a higher recurrence rate of MD (85%) than the general population (35%) (Hardeveld et al., 2010). These findings showed a noticeable proportion of MD patients fully recovered from the one and only MD episode they had.

Comorbidity of MD and other psychiatric disorders

Comorbidity describes the coexistence of more than one ailments (Feinstein, 1970) and it is a common phenomenon in mental disorders. It has been a huge problem in mental disorder diagnoses and treatments and the clinicians are interested in finding methods to distinguish mental disorders sharing similar symptoms because it is clinically challenging (Kapur et al., 2012).

The possible causes of comorbidity could be traced back to the development of the DSM and the ICD. The DSM was developed based on clinical experiences and it did not include explanations of disorders (Regier et al., 2009). Similarly, the development of the ICD was “a statistical classification of diseases and other health problems” (World Health Organization, 1992). The development of the classification systems may well justify why the classification systems do not include the underlying cause of the disorders but lacking such pivotal information might explain the prevalence of comorbidity in mental disorders. Clinical observations of syndromes, a group of correlated symptoms, are usually the initial stage of disease identification and follow by the discovery of pathology and etiology (Jablensky, 2016). However, a clear cut between syndromes and diseases remains missing among psychiatric disorders (Jablensky, 2016). This may contribute to the high comorbidity in mental disorders.

Comorbidity of several psychiatric disorders is common among patients and MD is no exception (Moscati et al., 2016; Thaipisuttikul et al., 2014). Comorbid psychiatric disorders are usually more severe than a single disorder (Kessler et al.,

2005). In most cases, the more psychiatric disorders one had the more severe are these disorders. Besides, having psychiatric disorders is the leading cause of suicide (Cavanagh et al., 2003) but comorbidity of mental disorders may not increase suicide risk. A Swedish study compared those who were diagnosed with severe MD and committed suicide with a matching group of controls who were diagnosed with sever MD but did not committed suicide (Heu et al., 2018). The two groups did not differ in the number of comorbid psychiatric disorders – whether there was/were one, two, three, or four different psychiatric disorders. Heu et al. (2018) concluded comorbidity of MD and other psychiatric disorders did not increase suicide risk.

It has been observed that MD is comorbid with several mental disorders including dysthymia, anxiety disorders, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, alcohol dependence, psychotic disorder, antisocial personality, and eating disorders (Thaipisuttikul et al., 2014). Among these comorbid psychiatric disorders, generalized anxiety disorder (GAD) is the most common comorbid disorder (Heu et al., 2018). Comorbidity between MD and anxiety disorder could be as high as 95% (T. A. Brown et al., 2001). High comorbidity between MD and GAD spurred the research question on which one of the two disorders comes first. A widely accepted argument was GAD preceded MD. This account was challenged and a study reported MD preceding GAD happened as frequent (Moffitt et al., 2007). The research into the two mental disorders revealed baseline MD significantly predicted GAD onset and vice versa (Kessler et al., 2008). However, while baseline GAD significantly predicted MD persistence, GAD persistence was not predicted by baseline MD. The researchers were also interested in whether the two disorders shared the same risk factors and whether they had the same underlying cause. Related studies reported conflicting results and risk factors including childhood adversities, parental history of mental disorders, and personality traits were observed to have varied influences on GAD and MD (Kessler et al., 2008). Moscati et al. (2016) found stressful life events and high neuroticism were indicators of MD and GAD comorbidity. Neuroticism has genetic correlations with internalized disorders such as MD and GAD (Hettema et al., 2006).

Heterogeneity of MD

MD overlaps with various psychiatric conditions. But is it a coherent entity itself or does it encompass a range of only loosely co-occurring symptoms? This is one of the central questions of this thesis.

The act of putting depressive symptoms together to form a medical diagnosis of MD implied a hidden assumption that these symptoms are homogeneous and their expressions are the clinical indicators of MD. Assuming homogeneity in MD symptoms legitimatize using the sum-total or the numbers of MD symptoms observed in patients to diagnose and determine MD severity in clinical practices. The MD diagnostic criteria in the DSM-V was reported to be able to clinically tell apart those who are not depressed from those who have the mild and severe form of MD (Tolentino & Schmidt, 2018). In this regard, the diagnostic criteria of MD could greatly help the clinicians to prescribe the patients with appropriate treatments. This assumption was challenged and some claimed MD is a heterogeneous disorder (Fried & Nesse, 2015b; Fried et al., 2014; D. Goldberg, 2011; Lux & Kendler, 2010). The claim of the heterogeneity of MD is based on the idea that the descriptions of several MD symptoms are opposite, such as insomnia vs. hypersomnia, weight loss vs. weight gain, and psychomotor agitation vs. psychomotor retardation. Depressive symptoms varied in their impacts on impairment in psychosocial functioning (Fried & Nesse, 2014), in the underlying biological mechanisms and in the degree they were affected by life events (Fried & Nesse, 2015b). Using data from 1,015 American Caucasian same-sex twins, Lux and Kendler (2010) tested the validity of DSM-IV diagnostic criteria of MD for each depressive symptom and two sets of symptoms – cognitive (depressive mood, loss of pleasure, guilt, and concentration problems, suicidal ideation) and neurovegetative symptoms (weight gain/loss, insomnia/hypersomnia, psychomotor agitation/retardation, and fatigue). Each symptom and the two sets of symptoms varied in their predictabilities of comorbidity with other psychiatric disorders, a new episode of MD or a MD diagnosis in a co-twin, man/woman, other demographics,

two personality traits – neuroticism and extraversion, duration of a MD episode and chronic depression, and historical MD episodes. Lux and Kendler (2010) concluded that instead of homogeneity, there is hidden heterogeneity among the depressive symptoms.

The heterogeneity of MD may also be illustrated by the heritability of each depressive symptom (Jang et al., 2004), highly diverse symptom patterns of MD (Fried & Nesse, 2015a), and different impacts of each MD symptom had on psychosocial functioning (Fried & Nesse, 2014). In a small group of Canadian twin participants, MD symptoms were explained by 14 genetic factors, where the heritability for each genetic factor varied greatly (Jang et al., 2004). The highly heritable factors are those associated with physiological functions (e.g., positive affect, insomnia, loss of pleasure, loss of appetite, suicidal ideation, and physical anxiousness). Other factors that were not heritable may be elicited by negative life events. A study found 1,030 possible unique symptom profiles in 3,703 MD patients (Fried & Nesse, 2015a) – there is a huge variety of ways to obtain a similar diagnosis! A review article presented evidences on MD symptoms differed in many aspects including underlying biology, risk factors, and their associations with difficult life events (Fried & Nesse, 2015b). These varied symptom profiles revealed a potential problem in clinical diagnosis - using the total sum-score of depressive symptoms may not be a reliable approach. Depressive symptoms had varying influences on the impairment of psychosocial functioning in work, home engagement, social activities, private activities, and close relationships, too (Fried & Nesse, 2014). The influences of the symptoms ranged from .7% (hypersomnia) to 20.7% (depressed mood). The impact of deeming whether MD symptoms are homogeneous or heterogeneous lies in its' influences on related research. It may hinder the well-being of patients as well as the progress of MD research.

The heritability of MD

The concept of "a gene for a trait" had been the central phrase of "GeneTalk" for a few decades (Kendler, 2005). The concept was supported by preformationist development models, where *anlagen* (preformed characteristics) gradually develop

and eventually become traits. However, the relationships between genes and psychiatric disorders are not that simple because many genes and the environment factors are involved. This implies the mechanisms of how genes caused psychiatric disorders may be complicated and lengthy. There have been many studies investigated the heritability of MD. Identifying loci for MD seemed to be particularly difficult compared to other mental disorders (Collins et al., 2011). Multiple loci contributing to the manifestation of MD may be one of the causes (Kendler et al., 2013; Sullivan et al., 2017). Another possibility is the heterogeneity of MD – several disorders sharing similar symptoms or different mechanisms produced similar symptoms (Flint & Kendler, 2014). Despite the limitations of genotyping techniques, the high cost, and small numbers of participants, a large number of loci associated with MD were reported in some studies although the individual effect sizes pertaining to each locus tend to be extremely small – depression is highly polygenic (CONVERGE consortium et al., 2015; Mbarek et al., 2017; Okbay et al., 2016). Contradicting findings were also reported and the possible solutions and problems of these contesting results were addressed in a review (Cohen-Woods et al., 2013). A genome-wide association meta-analysis study included data from seven cohorts with a large group of participants of 135,458 MD patients and 344,901 normal controls identified 44 independent loci (Wray et al., 2018). These findings showed heritability studies may contribute to the search for the underlying biological processes of MD. The involvement of a large number of genetic variants with small individual effect sizes is consistent with the etiologically heterogeneous nature of the condition.

The etiology of MD

The studies investigating the etiology of MD are from various aspects including genetics, molecular biology, neuroimaging, and a combined approach of genetic, molecular, and neuroimaging (Hasler, 2010; Kupfer et al., 2012). Patten (2015) proposed eight medical models to explain possible causes of MD. These models centered on internal biological causes of MD. The findings of these studies

not only pinpointed potential directions in the search of biomarkers but also broadened clinical treatment options.

Among the physiological indicators of MD, elevated hypothalamic-pituitary-adrenal (HPA) axis activity, which controls physiological responses of stress in human, has been found to be consistently related to MD (Juruena et al., 2018). An increase in cortisol level is an indicator of increased HPA axis activity. This association may be applied to explain the relationship between serotonin, stress and MD (Gotlib et al., 2008). Many of the broadly-prescribed antidepressants used in treating MD are designed to increase the amount of serotonin between neuron cells – synaptic clefts (Segi-Nishida, 2017). This type of antidepressants works on different mechanisms to increase serotonin level in the brain. Serotonin selective reuptake inhibitors (SSRI) is one of this type of antidepressants. It has several limitations including low efficacy, long therapeutic lag, and undesirable side effects including increase suicide risk (Gerhard et al., 2016; Kupfer et al., 2012). Ketamine has recently emerged to be a potentially effective and fast treatment for MD. Some reported it could decrease MD symptom severity in a few hours after administration and it was effective in treatment-resistant MD and bipolar depressed patients (Blynn G. Bunney & Bunney, 2012). The application of ketamine has been discussed extensively mostly due to its notorious history of abusive usage and psychomimetic side effects. The Food and Drug Administration in the U.S. had approved a new medication – nasal spray containing ketamine – to treat patients with treatment-resistant depression in March 2019 (Canady, 2019). In clinical treatment, switching between different antidepressants has been a common practice but this approach did not increase treatment effect as reported in a review article (Bschor & Baethge, 2010). In a review of MD treatments, however, treatment strategies including using augments, combining treatments, or switching antidepressants did not show lasting benefits (Connolly & Thase, 2011).

Antidepressants medication is commonly used in treating MD but there are pros and cons in antidepressant treatment. Antidepressants did not show specificity in treating different MD subtypes including atypical, melancholic, and anxious

depression (Arnow et al., 2015). A systematic review of 522 studies with 116,477 patients compared the efficacy of 21 antidepressants and found all the antidepressants were more effective in treating MD than placebo (Cipriani et al., 2018). However, a meta-analysis of 17 studies reported the antidepressants increased the mortality in MD patients who did not have pre-existing cardiovascular diseases by 33% (Maslej et al., 2017). But the mortality of MD patients with pre-existing cardiovascular diseases was not affected by antidepressants. Again, this is consistent with the etiologically heterogeneous nature of MD and may hint that its symptoms are to a substantial extent autonomous.

The efficacy and acceptability of antidepressants were studied and it was reported that the efficacy and acceptability of antidepressants in the head-to-head trials were greater than those in the placebo-controlled trials. Cipriani et al. (2018) observed greater dropout rate and smaller response to antidepressants in placebo-controlled trials and attributed these as a possible explanation for the disparity between placebo-controlled trials and head-to-head trials. The trustworthiness of head-to-head trials was challenged (Flacco et al., 2015). Among the 319 trials included in the analyses, 82.3% of the participants participated in trials were funded by pharmaceutical companies. Flacco and colleagues (2015) found 96.5% of the company-funded trials yielded results supporting the proposed treatments. Their results greatly challenged the credibility of these trials. An extensive discussion on the placebo response in antidepressant clinical trials produced several explanations and approaches to minimize the problem (Rutherford & Roose, 2013). These studies seemingly left the impression of new antidepressants are superior treatments than placebos and researchers should work towards minimizing placebo responses, which may be a potentially biased presumption.

Despite the progresses in various fields to understand MD, due to the heterogeneous nature of MD, the actual causes of MD remained obscure and no one single treatment could cure all MD patients.

Trans-diagnostic factors

Prevalent comorbidity, differences in disorder severity among patients, and missing biomarkers of mental disorders have increased the difficulties in treating mental disorders. Deducing symptoms to a few core symptoms shared by comorbid mental disorders – trans-diagnostic factors – may increase our understanding of mental disorders (Krueger & Eaton, 2015). The distinguishes between different mental disorders are obscure and unstable; therefore, adopting trans-diagnostic factors may provide a good alternative perspective in mental disorder research.

To distill trans-diagnostic factors, an internalizing-externalizing model is used. Mental disorders could be divided into internalizing and externalizing disorders based on the symptoms. MD belonged to the internalizing group together with GAD, panic disorder, and social and specific phobias etc. Based on this model, several symptoms could be used as potentially good trans-diagnostic factors were proposed – maladaptive repetitive thought (Kaplan et al., 2018) and distortions in metacognition (Rouault et al., 2018).

All these indications that the MD symptoms may be etiologically, descriptively and functionally heterogeneous points to the necessity to better understand the degree to which they operate separately as opposed to working in tandem. In this dissertation, I will mostly focus on short-term within-individual variability in depression symptoms to address the symptomatic heterogeneity of the condition. This can be efficiently done with modern mobile technology.

High-functioning MD

While many people have recurring MD episodes throughout their lives, many who used to have MD recovered from it and not only so. They even went on and achieved greatly both in their personal lives and at work (Rottenberg et al., 2018). According to Rottenberg et al. (2018), a strict definition of high end-state functioning after depression (HFAD) included three criteria – having a record of MD diagnosis, having fully recovered from MD with only minor or zero symptoms, and achieving high end-state functioning in various domains.

Experience Sampling Methodology (ESM)

Experience sampling methodology (ESM) has been widely used in studying various topics including daily activity, social interaction, changes in location, psychological states, and thoughts (Csikszentmihalyi & Larson, 2014). One advantage of ESM is that it allows the studying of participants' responses in real life settings. As a result, the data would have higher ecological validity compared to data collected in laboratories. In addition, using random sampling time scheme rather than a fixed sampling schedule also increases ecological validity by eliminating expectancy effect of future assessments due to previously completed questionnaires. Depending on the questions included, ESM enables the research into the inner processes of people's thoughts – "The objective is to identify and analyze how patterns in people's subjective experience relate to the wider conditions of their lives. The purpose of using this method is to be as 'objective' about subjective phenomena as possible without compromising the essential personal meaning of the experience" (Csikszentmihalyi & Larson, 2014, p. 37). The earliest ESM study could date back to as early as 1925 (Scollon et al., 2009). Despite the inconveniences, early researchers and participants managed to complete the ESM studies using pencil and papers, and phone calls. The advancement in communication technologies bring about devices such as pager, pre-programmed alarms, personal digital assistants, and smart phones, which greatly lower the technical and financial requirements to conduct ESM studies; therefore, ESM becomes an easily accessible methodology.

The strengths of ESM include high ecological validity, measuring the underlying psychological processes within individuals, and reducing memory bias (Scollon et al., 2009). Nevertheless, ESM studies are not without defects. The great demand ESM studies posit on participants – frequency and number of responses required from participants – may result in a highly-selective group of participants. The participants completed ESM studies may be those who are highly motivated, conscientious, and agreeable and whose professions, age, and lifestyle allow them to hear the notifications and to be interrupted at work whenever they are

prompted to answer the questions. These drawbacks limit the generalizability of the results of ESM studies. Possible solutions may be to explain the purpose of the study to the participants to establish trust and to create a "viable research alliance" (Csikszentmihalyi & Larson, 2014, p. 41), monetary incentives, and easing the burden of participants by decreasing the frequency and numbers of questions used in ESM studies.

ESM in mental disorder research

Viewing psychopathology as a dynamic construct of interwoven relationships between attributions, self-representations, and symptoms is suggested by Bentall, Corcoran, Howard, Blackwood, and Kinderman (2001). ESM is a good tool to assess the underlying dynamics of psychiatric disorders. And it has been used in clinical research (Bos et al., 2015; Lane et al., 2011; Myin-Germeys et al., 2009; Trull & Ebner-Priemer, 2014). A review of 18 studies in psychopharmacology demonstrated a broad application of ESM in various stages in psychopharmacology studies ranging from before, during, and after treatments (Bos et al., 2015). In these studies, ESM was used to collect baseline symptoms to be used in predicting treatment responses and outcomes before treatments and to detect exquisite changes in symptoms and the influences of the environments and treatment side effects during treatments. Later, the data was also applied to predict relapses after treatments.

ESM has been employed in MD research, too. An ESM study on MD reported people who experienced MD symptoms were more sensitive to social interactions (L. H. Brown et al., 2011). As a result, they would avoid social interactions with close friends even though these interactions may ease their MD symptoms – increase positive affect and decrease negative affect. Greater mood fluctuations were found in people with mild to moderate MD than those with severe MD (Nahum et al., 2017). A review of 42 ESM studies revealed risk and protective factors of depressed mood (Pemberton & Fuller-Tyszkiewicz, 2016).

This project

In this project, three ESM studies were conducted. These three studies were replicates of each other so that robust patterns or trends may be observed. The data of the three studies were analyzed separately because the data was collected at different times. Therefore, the analyses and writ-up of chapter sections were done at different times to complete the thesis in a timely manner.

Multiple variables and different analyses were used to compare MD symptoms to decipher the fine differences between MD symptoms – whether they are heterogeneous. Chapter 2 compares the inter-correlations between MD symptoms using retrospective and mean momentary MD ratings. Chapter 3 tests the predictability of MD severity and moderators including age, gender, educational attainment, employment status, and marital status on the variability of individual MD symptoms. Chapter 4 looks into whether MD symptoms vary in circadian rhythm and whether these variances correspond with MD severity. Chapter 5 checks the relationships between MD symptoms and personality traits and facets. Chapter 6 investigates how MD symptoms associate with activity level and heart rate variability. Chapter 7 examines the temporal, within- and between-subjects relationships among MD symptoms. Chapter 8 concludes and discusses the findings.

Chapter 2 Retrospective versus momentary assessments: using momentary ratings to validate retrospective ratings

Introduction

Retrospective assessments

Retrospective assessments are widely used by clinicians to diagnose illnesses. Depending on the specific designs and purposes, assessments used to measure the same phenomenon may differ in recall periods such as those used to measure pain and fatigue symptoms (e.g., 4-week, 1-week, one-day, at rest and during activity, or hourly, morning, evening, and mean, or current recall) (Broderick et al., 2008; Litcher-Kelly et al., 2007). One possible explanation why retrospective assessment is the predominant form of assessment may be: for any condition to be considered as with medical relevance, and therefore worth medical attention, clinical diagnosis and treatment, it should last at least a prolonged period of time. Retrospective assessments are thought to be good at capturing these particular features than momentary assessments because they require respondents to mentally aggregate what has been typical for them over an extended duration. Another possible explanation might be because retrospective assessments are the most available and convenient way to evaluate a condition. Clinicians can easily estimate patients' illness levels based on their retrospective ratings and, hopefully, render appropriate medical assistances or treatments. Despite these strengths, this method still has some drawbacks. Bhandari and Wagner (2006) reviewed 42 papers on self-reported utilization of health care services and concluded that the accuracy of self-reports were influenced by six factors – recall timeframe, type of health care service, frequency of utilization, questionnaire design, mode of data collection, and memory aids.

The symptoms of major depression (MD) are diverse. Using retrospective assessments as the sole measurement may limit the scope the symptoms could be measured because there is only so much people can remember or can be asked

about. This may forsake the possibilities of discovering symptoms that are not covered in the retrospective assessment instruments. For example, the diagnostic criteria for MD in the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM) only partially include or did not include some depressive symptoms mentioned in Psychiatry or Psychological medicine textbooks (Kendler, 2016). The partially included symptoms are depressed mood or irritable and guilt/worthless and the symptoms not included are volition/motivation, problem in speech, anxiety, physical symptoms (e.g., headaches, aches and pains), and depersonalization/decreolization. All of these symptoms except depersonalization/decreolization could be measured using retrospective assessments because it is "a subtle concept, time-consuming to evaluate, and perhaps of limited reliability" (Kendler, 2016, p. 778). The two symptoms that were partially included in the DSM-V have a broad range of descriptions. The descriptions for depressed mood or irritable are "depressed, melancholy, blue, sad, lonesome, worried, homesick, and noted in the facial expression" and those for guilt/worthless are "self-derogatory, self-depreciatory ideas, ideas of unworthiness, guilt, sin, the source of trouble for others" (Kendler, 2016, p. 777). However, the range of depressive symptoms that retrospective assessment instruments collectively covered is diverse but each instrument covered only a small subset of these symptoms (Fried, 2017).

Long vs. short recall periods

Validity and reliability of assessments are crucial because they determine whether the results of these assessments are trustworthy. Also, "a respondent's ability to accurately report their experiences" and "forgetting and differential forgetting are mechanisms which produce misclassification error" (Donald E. Stull et al., 2009, p. 930; Wells & Horwood, 2004, p. 1008). These implied potential problems of retrospective assessments and recall periods used in retrospective assessments may influence the validity and reliability of the assessments and result in unforeseen issues.

The results of assessments with long recall periods are usually less accurate compared to the assessments with short recall periods because recall biases increased with the increase in recall periods (Broderick et al., 2008). However, while short recall periods are excellent in detecting momentary fluctuations, using only short recall periods in assessments may not be the most optimal approach. Frequent assessments may not catch crucial events, which usually take time to manifest; therefore, these events could be captured by using repeated assessments with longer gaps or retrospective assessments whereby respondents mentally aggregate symptoms and events happened over a period. For example, since medication adherence usually stabilize over time, measuring AIDS patients' medication adherence by using an assessment with a long recall period would be more accurate than using the same assessment with a short recall period (Lu et al., 2008). When selecting the most appropriate recall period to be used in an assessment, researchers should base their decisions on the variability of the target phenomenon (Keller et al., 1997; Donald E. Stull et al., 2009). To investigate a frequently changing phenomenon, adopting a short recall period with repeated assessments or momentary assessments may be more promising in capturing a full picture of that phenomenon than using assessments with long recall periods. In addition, depending on the duration of a phenomenon, the assessment period is crucial to uncover the features of the target phenomenon. If the duration of the target phenomenon is short, researchers could easily gather enough information to put together the puzzle behind the target phenomenon simply by using an assessment with a short recall period. But if the target phenomenon lasts relatively long, a more assuring approach to unveil the hidden aspects of the target phenomenon would be to employ assessments with long recall durations (Donald E. Stull et al., 2009).

Peak-end rule

One well-studied phenomenon that may cause biases in retrospective assessments is the peak-end rule. Specifically, the nature of this phenomenon is that people's memories of own peak (the most salient experiences of events) and

end (the experiences of the end of events) experiences for certain events are more outstanding than their memories of other parts of these events. Peak-end rule has been observed in people suffering from chronic pain (Stone et al., 2000), university students' affective experiences in watching a film (Fredrickson & Kahneman, 1993), in elementary, middle school, and undergraduate students' evaluations of material goods (Do et al., 2008), and in patients' experiences of invasive medical examinations (Redelmeier & Kahneman, 1996). However, the results of the studies measuring affective experiences for a prolonged period (e.g., one week) did not support the peak-end rule. For positive and negative affect, the averages of momentary ratings were superior predictors of retrospective ratings than the means of the peak and end ratings in both normal and depressed participants (Ben-Zeev et al., 2009) as well as in university students (S. Kemp et al., 2008). These inconsistent findings might result from the long measuring period, which may increase recall bias. Also different from the studies on peak-end rule, where participants were asked to rate a specific experience (e.g., arthritis pain and pain experienced while undergoing colonoscopy and lithotripsy), participants were asked to rate their general feelings.

Recall of depressive symptoms in people with depression

People with depression generally have poor memories of their previous depressive symptoms. A New Zealand birth cohort study showed among people with depressive symptoms and people who met the diagnostic criteria of depression, only 22% and 44% remembered their previous key depressive symptoms, respectively (Wells & Horwood, 2004). Also, a study on lifetime depressive episode reports showed 57.5% of the people who had depressive episodes during their participation of the study (the 1st, 2nd, 3rd, and 4th interviews) did not remember having depressive episodes in the final interview (the 5th interview) (Aneshensel et al., 1987). The discrepancies were mostly on reporting having depressive episodes in previous interviews but did not report having depressive episodes in the last interview (86%). The remaining different reports were from participants who did not report any depressive episodes between the 1st

and the 4th interviews but reported having depressive episodes in the last interview (14%). A study comparing positive and negative affect of healthy controls and people with depression found both groups tended to exaggerate positive and negative affect (Ben-Zeev et al., 2009). However, while healthy controls over-reported their positive affect more than their negative affect, depression patients did not overstate their negative affect more than their positive affect.

Although having poor recall of previous depressive episodes or symptoms is common among people with MD, some patients recalled better than others. People who had superior recall were also those who had been severely depressed, had been diagnosed with depression for three or more years, had suicidal ideation for three or more years, were currently depressed, were females, and had received depression treatments before they were 21 years old (Aneshensel et al., 1987; Kendler et al., 2001; Wells & Horwood, 2004). This may be explained by a phenomenon in memory processing, "state-dependence", where current depression experiences may remind people having depression their previous symptoms and not having depressive symptoms may cause people to forget their past symptoms (Aneshensel et al., 1987; Blaney, 1986; Bower, 1987; Kendler et al., 2001).

Momentary assessment

In contrast to retrospective assessments, momentary assessments measure real-time features of a phenomenon and are not subject to memory biases. Instead of rating what had happened in the past, respondents are asked to rate their feelings at the moment. As mobile technology becomes more mature and available to the general public, the time has come and the tools supporting momentary assessments have become more available than ever before. This provides researchers a great opportunity to compare and to research into the differences between retrospective and momentary measures. In a study on pain and fatigue patients, Broderick et al. (2008) compared the means of momentary ratings, which were measured seven times a day, and the retrospective assessments were measured across various recall periods including one day, three days, seven days,

and 28 days. In their report, the accuracy of retrospective ratings was measured by the correlations between momentary and retrospective ratings. The accuracy of retrospective ratings was influenced by the length of recall periods. The retrospective ratings were greater than the mean momentary ratings and increased as the recall period lengthened. The accuracy of retrospective ratings was higher for shorter recall periods and lower for longer recall periods, where the one-day recall was the most accurate and the seven-day recall was the least accurate. Surprisingly, in some items, the accuracy of the 28-day recall was not the least accurate among the various recall periods and its accuracy was greater than the seven-day recall.

The decline in recall accuracy as the increase in the recall period revealed a potential issue in retrospective assessments. As mentioned earlier, retrospective assessments are widely used in medical practice and if they are unreliable indicators, basing diagnoses on these assessments would be problematic. Hence, this study adopted the Experience Sampling Methodology (ESM) and retrospective assessments to compare the momentary and retrospective assessments of MD to explore the differences between the two types of assessments.

Study design

Considering that both retrospective and momentary assessments have their strengths and weaknesses, three studies adopted both retrospective and momentary assessments to measure MD symptoms to compare the means of the momentary assessments with the retrospective assessments. Because the measurements were taken relatively frequently in the momentary assessments, this opens a door to observe the symptom variability within MD symptoms. In addition, if the total duration of momentary assessments and the recall period of retrospective assessments are long enough, the cycle of MD including the manifestation, duration, and the characteristics of different phases of MD could also be depicted. However, due to a practical issue – long period may decrease participant compliance and participants' willingness of participation, the durations of data collection were 15 days in Study 1 and 14 days in Studies 2 and 3.

In this present study, depressive symptoms were firstly measured using retrospective assessment at the beginning of the study, followed by 15-day (Study 1) or 14-day (Studies 2 and 3) momentary assessments, and then a retrospective assessment at the end.

Although retrospective assessments have their advantages and are the most widely used type of assessment, sometimes the accuracy of these assessments are questionable because of recall biases. Recall periods could greatly affect recall bias, where the longer the recall periods are, the less precise are the results. Previous studies have shown people tend to base their responses on their peak and end experiences of events. Nevertheless, momentary assessments are less subject to recall biases because instead of asking people to recall how they felt in the past, people are asked to answer questions based on their feelings at the moment. When combined with multiple sampling times design, momentary assessments are also good tools to measure highly variable constructs such as MD symptoms.

The diagnostic criteria of MD include nine diverse symptoms. Although MD may affect different parts of the body therefore various symptoms are observed, people who have MD usually have different symptoms or other conditions (e.g., somatic symptoms, panic attacks, obsessional traits, physical illnesses, or dementia) (D. Goldberg, 2011). These constitute the heterogeneous nature of MD. In addition, the nine symptoms have varied levels of discriminant ability to distinguish people have MD from those do not have MD (McGlinchey et al., 2006). This raised a question of how similar or how different are the nine symptoms and how much could the retrospective assessments of MD distinguish the differences between the symptoms.

The studies

In this chapter, we tested the following hypotheses. H1: The correlations between items measuring different symptoms in retrospective and momentary assessments (discriminant validity) should, on average, be significantly smaller than those items measuring the same symptoms (convergent validity). H2: According to the peak-end rule, the means of the peak (the 75th percentiles of momentary

ratings) and the end ratings (the means of momentary ratings obtained on the last sampling day) of the momentary assessment should be more highly correlated with the retrospective ratings than the overall mean ratings of the momentary assessments. H3: Also, based on the peak-end rule, if end experiences taint the retrospective memory, the mean ratings of the second half of the sampling period should be superior predictors of the retrospective ratings to the means of the first half momentary ratings. H4: If MD symptoms fluctuate substantially over time and the momentary assessments could capture the fluctuations of MD symptoms (and not just fluctuations of underlying MD), then the inter-symptom correlations among retrospective ratings would be greater than those among the momentary ratings.

In three studies, we employed a widely used retrospective measure of depression, the Patient Health Quality-9 (PHQ-9) and developed a momentary measurement, the Daily Depression Items, (DDI) based on the Zung Self-Rating Depression Scale (Zung, 1965), the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983), and the Depression Anxiety Stress Scales (Lovibond & Lovibond, 1996). There were minor modifications of the DDI used in Studies 2 and 3. The mapping of the two measurements according to the DSM-V diagnostic criteria of MD was listed in Table 2.1. All *p*-values in the three studies were adjusted for multiple comparison using false discovery rate (FDR). Compared to Bonferroni correction, FDR is more lenient thus may avoid the possibility of falling into Type II error and yield robust results (Benjamini & Hochberg, 1995; Xie et al., 2011).

Table 2.1 *Mapping of the DSM-V diagnostic criteria for MD onto the momentary and retrospective assessments*

MD in the DSM-V	Retrospective assessment (PHQ-9)	Momentary assessment (DDI)
Depressed mood or irritable	Feeling down, depressed, or hopeless	I feel sad.** I feel irritable.* I feel happy. **
Decreased interest or pleasure	Little interest or pleasure in doing things	I enjoy what I am doing. I don't care about anything.
Significant weight change (5%) or change in appetite	Poor appetite or overeating	I have no appetite during the day.
Change in sleep	Trouble falling or staying asleep, or sleeping too much	I didn't have enough sleep last night.** I worry about sleeping.
Change in activity	Moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual	I am restless. It is not effortful to do things.** I am doing things with my normal pace.*
Fatigue or loss of energy	Feeling tired or having little energy	I am tired.
Guilt or worthlessness	Feeling bad about yourself - or that you are a failure or have let yourself or your family down	I feel worthless. I feel that I can't get anything done.** I feel guilty.**
Concentration	Trouble concentrating on things, such as reading the newspaper or watching television	I can't concentrate. I feel that I can’t make decisions.**
Suicidality	Thoughts that you would be better off dead of or hurting yourself in some way	I feel hopeless.
		How's your day? How would you rate your overall physical health today?* What time did you go to bed last night?** What time did you wake up this morning?**

Note. * Revised or newly added items in Study 2; ** newly added or revised items in Study 3.

Study 1

Materials and Method

Participants

Participants were recruited from on-line advertisements on an internal job searching website of the University of Edinburgh, invitation e-mails were sent to those who participated in other studies held in the Department of Psychology previously and indicated interests of participation in future studies, and an undergraduate student subject pool. In total, 238 participants expressed their interests in participating in this study by signing up on-line and completed the initial retrospective assessment (177 females and 61 males with mean age of 25.56 years and *SD* of 11.55 years), 153 participants partially completed or fully completed the momentary assessments, and 128 completed the final retrospective questionnaire. Among those, the following participants were removed from further analysis: two answered the momentary assessments carelessly as shown in the correlations among the questions, where there should be both positive and negative correlations because of several reverse-scoring items, but only positive correlations were observed in these two participants, and 109 participants did not complete the study due to personal reasons or technical problems (e.g., unable to couple their phones successfully). The following duplicated data were removed: two participants completed the initial retrospective assessment twice and one participant answered the final retrospective assessment twice. In addition, as a result of incomplete data, 981 momentary observations were excluded from further analyses. The remaining 127 participants (97 females and 30 males) completed this study and provided momentary data of 6392 time-points in total. The mean age of those who completed Study 1 was 24.87 years (*SD* = 10.6). After completing the study, participants recruited from the undergraduate subject pool received course credits and participants recruited from other places received either £5 cash or a £5 Tesco digital gift card as compensation. All participants also received a general personalized feedback of the correlations of the momentary measures. Participants

were not notified whether their scores on the PHQ-9 exceeded the diagnostic threshold for MD.

Materials

The Patient Health Quality of Somatic, Anxiety, and Depression Scale (PHQ-SADS) was used to measure baseline depressive symptoms along with other symptoms or conditions relevant to depression. The PHQ-SADS consisted of the PHQ-9, General Anxiety Disorder-7, and Patient Health Questionnaire-15 with a total number of 37 items. A study measured the validity of the PHQ-9 in 6,000 patients with the 20-item Short-Form General Health Survey as an assessment for construct validity and the mental health professional re-interview as the criterion standard, the results showed a PHQ-9 score of 10 or more indicates a sensitivity of 88%, a specificity of 88%, and a positive likelihood ratio of 7.1 (Kroenke et al., 2001). Personality traits were measured using the 120-item International Personality Item Pool (IPIP) (L. R. Goldberg, 1999; L. R. Goldberg et al., 2006; J. A. Johnson, 2014). These personality data will be used in Chapter 5. The DDI was used to measure real-time changes of depressive symptoms. A full list of the items in the DDI was shown in Table A.3 in Appendix A.

Procedure

After participants indicating their interests of participating in this study by signing up on-line, they were directed to fill in the first on-line retrospective assessment comprising several demographic questions, the PHQ-SADS, and the IPIP. The consent form was part of the on-line sign-up form. Later, a researcher e-mailed them the instructions on preparing their Android smart phones including downloading and installing an app, movisensXS (Movisens GmbH), on their phones. Those who did not have an Android smart phone used our lab phones to participate. movisensXS has been used in several studies such as personality (R. Mõttus et al., 2016; Wrzus & Mehl, 2015), stress (Stütz et al., 2015), and the compliance of disadvantaged elderly people to ecological momentary assessment studies (Fritz et al., 2017).

A day after participants' successfully set up their Android smart phones, they started to receive notifications to respond to the DDI four times per day over 15 days. The participants' responses were collected once in the mornings, twice in the afternoons, and once in the evenings. The notifications during weekdays was between 8 A.M. and 10:30 P.M. and between 9 A.M. and 11 P.M. during weekends. After the participants completed the momentary assessments, a researcher e-mailed them the final instructions on uploading the remaining responses and a link to complete the second retrospective assessment. The data collected in this second retrospective assessment was used as the retrospective ratings mentioned in this thesis.

Results

The number of momentary questionnaires included in analyses was 6,372. The descriptive characteristics of the participants were listed in Table 2.2. Participants' momentary ratings of the reverse scoring items were adjusted by subtracting the ratings from 100, which is the highest rating on the scale. The distribution of momentary MD symptoms in each participant varied substantially as shown in the means and standard deviations of all momentary ratings across participants in Table 2.3. The correlations between the retrospective and momentary assessments were analyzed by comparing the retrospective ratings obtained after participants completed the momentary assessments with the mean momentary ratings. The Spearman's rank-order correlation was used to test this because the original data was non-parametric. The Spearman's rhos were shown in Table 2.4. All items were positively correlated and most correlations were significant.

Table 2.2 *Descriptive characteristics of the participants*

	Study 1 (*n* = 127)	Study 2 (*n* = 75)	Study 3 (*n* = 78)
Age, *M* (*SD*)	24.87 (10.6)	20.51 (3.31)	25.46 (6.18)
Sex, *n* (%)			
Female	97 (76)	57 (76)	57 (73)
Male	30 (24)	18 (24)	21 (27)
Education, *n* (%)			
GCSE	1 (1)	0 (0)	2 (2.6)
A level/Highers	58 (46)	46 (61)	25 (32)
Bachelor's degree	33 (26)	16 (21)	20 (25.6)
Master's degree	32 (25)	12 (16)	24 (30.8)
PhD	3 (2)	1 (1)	7 (9)
Marital status, *n* (%)			
Single	77 (61)	56 (75)	54 (69)
Married	9 (7)	1 (1)	4 (5)
Divorced	3 (2)	1 (1)	2 (3)
In a relationship	38 (30)	17 (23)	18 (23)
Employment status, *n* (%)			
Employed or self-employed	5 (4)	1 (1)	9 (11.5)
Part-time employed	12 (9)	7 (9)	6 (7.7)
Full-time student	86 (68)	59 (79)	60 (77)
Retired	7 (6)	0 (0)	0 (0)
Unemployed	17 (13)	8 (11)	3 (3.8)

Note. For the employment status in Study 1, five participants did not select the specified categories and were re-categorized to fit in the existing categories. These are one participant identified himself/herself as an underemployed freelancer was included in part-time employed, two participants identified himself/herself as a student and one participant regarded himself/herself as paid to be a full-time PhD student were included in full-time student, one participant who claimed that he/she will be employed at the end of June was included in unemployed.

Table 2.3 *Means and SDs of the DDI items in Studies 1, 2, and 3*

DDI item	*Mean*			*SD*		
	Study 1	Study 2	Study 3	Study 1	Study 2	Study 3
I feel happy.	-	-	34.44	-	-	22.06
I feel sad.	32.83	31.02	26.29	21.97	21.35	23.60
I feel irritable.	36.47	29.22	28.57	23.56	21.67	24.28
I enjoy what I am doing.	34.01	33.40	32.94	23.05	21.87	23.73
I don't care about anything.	28.45	27.43	26.43	21.93	20.12	25.80
I have no appetite during the day.	26.69	29.39	23.52	24.75	22.50	22.70
I worry about sleeping.	38.35	39.88	32.82	30.19	28.05	28.78
I didn't have enough sleep last night.	46.73	45.31	41.96	30.96	28.98	30.62
I am restless.	39.12	35.82	32.01	26.65	24.03	26.65
I am tired.	51.49	50.19	47.06	29.40	26.94	28.55
It is not effortful to do things.	54.95	50.12	-	26.78	25.45	-
I feel guilty.	-	-	29.63	-	-	30.38
I am doing things with my normal pace.	-	9.03	10.66	-	11.93	12.11
I feel worthless.	29.73	29.69	24.40	24.92	22.80	26.71
I feel that I can't get anything done.	43.91	40.33	-	27.73	23.06	-
I feel that I can’t make decisions.	-	-	28.92	-	-	24.56
I can't concentrate.	42.82	40.58	35.72	27.12	22.85	26.60
I feel hopeless.	31.49	31.89	26.24	24.40	22.65	26.30
How's your day?	35.28	37.35	34.98	24.04	22.38	23.02
How would you rate your overall physical health today?	-	40.70	37.63	-	23.41	25.54

Table 2.4 *Spearman's rhos between the PHQ-9 and DDI items in Study 1*

DDI item \ PHQ-9 item	Little interest	Feeling down	Trouble in sleep	Tired	Altered appetite	Feeling bad about self	Concentration problem	Psychomotor changes	Suicidal ideation
I feel sad.	.47***	.58***	.43***	.47***	.43***	.56***	.38***	.32***	.48***
I feel irritable.	.47***	.57***	.45***	.49***	.45***	.54***	.40***	.34***	.46***
I enjoy what I am doing.	.48***	.55***	.48***	.49***	.46***	.54***	.42***	.32***	.45***
I don't care about anything.	.41***	.39***	.32***	.26**	.32***	.33***	.22*	.27**	.33***
I have no appetite during the day.	.36***	.38***	.32***	.35***	.35***	.33***	.23*	.19*	.34***
I worry about sleeping.	.43***	.51***	.56***	.54***	.46***	.53***	.36***	.23*	.42***
I feel that I didn't have enough sleep last night.	.37***	.35***	.59***	.59***	.41***	.41***	.40***	.27**	.32***
I am restless.	.41***	.48***	.35***	.45***	.45***	.47***	.45***	.33***	.32***
I am tired.	.40***	.46***	.49***	.60***	.46***	.44***	.47***	.27**	.36***
It is not effortful to do things.	.32***	.34***	.36***	.38***	.20*	.38***	.43***	.15	.14
I feel worthless.	.57***	.73***	.48***	.55***	.48***	.72***	.50***	.40***	.48***
I feel that I can't get anything done.	.51***	.51***	.51***	.56***	.39***	.55***	.57***	.26**	.31***
I can't concentrate.	.50***	.51***	.52***	.59***	.48***	.60***	.61***	.26**	.31***
I feel hopeless.	.55***	.68***	.50***	.54***	.52***	.66***	.46***	.40***	.49***
How's your day?	.47***	.55***	.44***	.47***	.39***	.52***	.34***	.29**	.46***

Note. Little interest = little interest or pleasure in doing things; feeling down = feeling down, depressed, or hopeless; trouble in sleep = trouble falling or staying asleep, or sleeping too much; tired = feeling tired or having little energy; altered appetite = poor appetite or overeating; feeling bad about self = feeling bad about yourself – or that you are a failure or have let yourself or your family down; concentration problem = trouble concentrating on things, such as reading the newspaper or watching television; psychomotor changes = moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual; suicidal ideation = thoughts that you would be better off dead of or hurting yourself in some way. * $p < .05$. ** $p < .01$. *** $p < .001$.

We firstly examined the discriminant and convergent validity of the retrospective and the momentary questionnaires by comparing the correlations among items measuring the same and different MD symptoms in the DSM-V diagnostic criteria using the Wilcoxon rank-sum test. The Spearman's correlations between the mean momentary ratings and the retrospective ratings were calculated and then these values were transformed to z scores by using Fisher's approach before analyzing in the Wilcoxon test. The medians of Spearman's rhos for the items measuring the same and different MD symptom were .56 and .44, respectively, and the two groups of the Spearman's rhos transformed z scores were significantly different according to the Wilcoxon rank-sum test (W = 1204, p = .014). This indicated the items measuring the same MD symptoms showed higher convergence across rating methods (momentary vs retrospective) than did those measuring different MD symptoms, therefore supporting H1. This suggests that, generally, retrospective ratings are, at least to some extent, able to discriminate among depressive symptoms as perceived "real time".

The peak-end rule was tested by transforming the correlation coefficients between retrospective ratings and momentary ratings into z scores and then comparing the z scores in pairs using the Wilcoxon signed rank test. Specifically, in order to test the peak-end rule, we compared the correlations between the retrospective ratings and four different momentary ratings – the mean momentary ratings, the peak momentary ratings, the end momentary ratings, and the peak-end ratings (the averages of the peak and the end ratings of the momentary assessment). The Wilcoxon signed rank test was used to analyze the six pairs of comparisons – a) the mean momentary ratings vs. the peak momentary ratings, b) the mean momentary ratings vs. the end momentary ratings, c) the mean momentary ratings vs. the peak-end momentary ratings, d) the peak-end momentary ratings vs. the peak momentary ratings, e) the peak-end momentary ratings vs. the end momentary ratings, and f) the peak momentary ratings vs. the end momentary ratings indicated significant differences between all the pairs (ps < .05) (Table 2.5). The medians of Spearman's rhos indicated the peak-end

momentary ratings correlated greater with the retrospective ratings (.43) than the end momentary ratings did (.38). However, the associations between the mean momentary ratings and the retrospective ratings (.45) and between the peak momentary ratings and the retrospective ratings (.44) were higher than those between the peak-end momentary ratings and the retrospective ratings. H2 was rejected.

Table 2.5 *The estimates and p-values of Wilcoxon signed rank test between retrospective ratings and four momentary ratings – the mean momentary ratings, peak-end momentary ratings, peak momentary ratings, and end momentary ratings and the medians of the Spearman's rhos of the four momentary ratings in Studies 1, 2, and 3*

Momentary ratings and comparisons	*V*			*p*-value			Median of Spearman's rhos		
	1	2	3	1	2	3	1	2	3
Mean							.45	.25	.44
Mean vs. Peak	5403	5788.5	8779	< .001	.089	< .001			
Mean vs. End	7558.5	8503.5	8108	< .001	< .001	< .001			
Mean vs. Peak-end	4433	6597	5474	.029	< .001	.547			
Peak-end							.43	.24	.42
Peak-end vs. Peak	4469.5	3913.5	2911.5	.053	.001	< .001			
Peak-end vs. End	368	8434	1790	< .001	< .001	< .001			
Peak							.44	.25	.41
Peak vs. End	7005	7990.5	6409.5	< .001	< .001	.294			
End							.38	.18	.40

Note. 1 = Study 1; 2 = Study 2; 3 = Study 3.

Whether people's memories of MD symptoms were more highly related to the means of the first half momentary ratings or the means of the second half momentary ratings was tested by using Wilcoxon signed rank tests. The first half momentary ratings were the momentary ratings recorded before the median of all momentary assessments in each participant. The remaining momentary ratings were the second half momentary ratings. The results showed the momentary ratings of the first and the second sampling week were significantly different (*V* =

5096, p = .004). The medians of the Spearman's rhos of the first half momentary ratings and the second half momentary ratings were .43 and .41, respectively. This showed the first half momentary ratings correlated greater with the retrospective ratings than the second half momentary ratings. When asked to retrospectively rate their feelings, the participants referenced their experiences of the first half of the sampling period more than their responses of the second half of the sampling period (end experience). H3 was rejected.

We further examined whether the inter-correlations among MD symptoms were stronger in the average momentary or retrospective assessments using the principal component analysis (PCA). The results showed the mean momentary ratings of MD symptoms revealed a slightly more uniform symptom structure than the retrospective assessments. The loadings ranged from .59 to .85 and from .45 to .93 in the retrospective and the average momentary assessments, respectively. Table 2.6 shows the PCA loadings for the DDI and PHQ-9. The first principal components of the retrospective assessments explained 57 percent and those in the average momentary assessment explained 62 percent of the total variance among the variables. The medians of the Spearman's rhos of the inter-correlations between retrospective ratings and between the mean momentary ratings were .51 and .56, respectively. This showed the items in the momentary assessment correlated slightly greater than those in the retrospective items.

Table 2.6 *PCA Loadings for the DDI and PHQ-9 items in Studies 1, 2, and 3*

DDI item	Mean ratings			First ratings		
	1	2	3	1	2	3
I feel happy.	-	-	.89	-	-	.66
I feel sad.	.91	.86	.86	.76	.52	.73
I feel irritable.	.91	.79	.69	.74	.40	.40
I enjoy what I am doing.	.93	.82	.87	.61	.56	.43
I don't care about anything.	.70	.55	.73	.56	.11	.50
I have no appetite during the day.	.62	.58	.67	-	-	-
I worry about sleeping.	.63	.49	.33	-	-	-
I didn't have enough sleep last night.	.69	.40	.39	.63	.48	.46
I am restless.	.65	.74	.67	.47	-.01	.34
I am tired.	.77	.42	.60	.66	.56	.51
It is not effortful to do things.	.45	.55	-	.34	.58	-
I feel guilty	-	-	.79	-	-	.46
I am doing things with my normal pace.*	-	.34	.43	-	0	.29
I feel worthless.	.87	.79	.88	.76	.41	.70
I feel that I can't get anything done.	.82	.76	-	.71	.58	-
I feel that I can’t make decisions.	-	-	.86	-	-	.53
I can't concentrate.	.85	.73	.86	.68	.66	.58
I feel hopeless.	.91	.85	.90	.79	.88	.54
How's your day?	.89	.64	.87	-	-	-
How would you rate your overall physical health today?*	-	.67	.65	-	-	-
PHQ-9						
Little interest or pleasure in doing things	.80	.68	.72			
Feeling down, depressed, or hopeless	.83	.78	.79			
Trouble falling or staying asleep, or sleeping too much	.79	.67	.73			
Feeling tired or having little energy	.85	.75	.79			
Poor appetite or overeating	.68	.71	.67			
Feeling bad about yourself - or that you are a failure or have let yourself or your family down	.81	.80	.76			
Trouble concentrating on things, such as reading the newspaper or watching television	.76	.69	.73			
Moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual	.59	.52	.62			
Thoughts that you would be better off dead of or hurting yourself in some way	.67	.68	.73			

Note. 1 = Study 1; 2 = Study 2; 3 = Study 3.

Although the difference was marginal, the higher inter-correlations among the mean momentary ratings could reflect their higher reliability (because they were aggregated across multiple measurement occasions). To rule out this alternative explanation, the correlations among the very first momentary ratings and the retrospective ratings were also compared. The loadings ranged from .34 to .79 and the first principal components of the first momentary ratings explained 43 percent of the total variance among the variables. These indicated there were no stronger inter-correlations among items in the momentary assessment – in fact the opposite. The median of the Spearman's rhos of the first momentary ratings was .37, which was smaller than those of the mean momentary ratings and the retrospective ratings as mentioned in the previous paragraph. The weak inter-correlations implied the participants' first momentary ratings varied hugely and supported H4. This revealed the highly variable nature of MD symptoms.

To examine the results of Study 1, we conducted Study 2 as a replicate of Study 1 and included minor modifications. The major modification was adopting a different mobile phone application in data collection. In Study 1, movisensXS was the primary tool to collect momentary data but there was a problem of excluding participants using iPhone Operation System (iOS) devices including iPhones and iPads because movisensXS could only be installed in Android tablets or phones. Although we offered the iOS users an option of using our lab phones to participate, this was still not an optimal approach to recruit iOS users, therefore we conducted Study 2 to include iOS users.

Study 2

Materials and Method

This study was a replicate of Study 1 with minor modification to test the robustness of the results of Study 1. MovisensXS, the Android mobile phone application used in Study 1 was replaced with Qumi to include iOS users, some questions on participants' lifestyle were included in the initial retrospective

questionnaire to test potential factors influencing mood, and three items in the DDI were modified or added.

Participants

Participants were recruited via the same approaches as those used in Study 1. In total, 230 participants signed up for Study 2, data from 78 participants were collected. However, three participants did not complete the final retrospective assessment and only 75 participants (57 females and 18 males) fully completed this study (mean age = 20.51 and *SD* = 3.31).

Materials

Several lifestyle questions including questions asking participants' diet, smoking, drinking, and exercising habits, and medical history (physical illnesses and psychiatric disorders) were included to control for variables influencing MD symptoms. Also, one anchoring point of the item, "I feel irritable", in the DDI was revised from "cheerful" to "calm". Two items were added. They were Items 11 "I am doing things with my normal pace" with anchor points of "faster", "normal", and "slower" and Item 17 "How would you rate your overall physical health today" with anchoring points of "very good" and "not very good". The other items in the DDI were the same as those used in Study 1 (Table A.4 in Appendix A).

Procedure

A procedure similar to that used in Study 1 was used. When the participants signed up on-line, they were asked to read and agree to the consent form before providing their e-mail addresses. Once the participants had signed up to participate in this study, the researcher of this study sent them instructions on how to set up their mobile phones, which included downloading and installing Qumi and loading the questionnaire file. Different from Study 1, where participants completed the momentary and retrospective assessments on two different platforms, movisensXS and Google Forms, respectively. In this study, all questionnaires were administered in Qumi and the researcher did not have access to participants' responses until the participants e-mailed their responses to the researcher. The participants were asked to answer six mobile questionnaires per day over 14 days.

Results

A total of 3,955 momentary questionnaires were used in analyses. Technical problem was a major reason of participants missing questionnaires, where the participants did not receive notifications to fill out the momentary questionnaires. Table 2.2 shows the descriptive characteristics of the participants. During data preparation, all momentary ratings of four reverse scoring items were adjusted in the same way as in Study 1. The momentary ratings of the newly added item in this study – "I am doing things with my normal pace", which had three anchoring points of "Faster", "Normal", and "Slower" – were adjusted by subtracting the ratings from 50 and then converting to absolute values. Compared to the variabilities of momentary MD symptoms in Study 1, participants in Study 2 varied less in their momentary ratings because the SDs of all items were smaller than those in Study 1. Also, the mean momentary ratings of most items in Study 2 were also smaller than those in Study 1. The means and SDs of all momentary ratings were shown in Table 2.4. Consistently with Study 1, the correlations between all items were positive and the majority were significant (Table 2.7).

Table 2.7 *Spearman's rhos between the PHQ-9 and DDI items in Study 2*

DDI item \ PHQ-9 item	Little interest	Feeling down	Trouble in sleep	Tired	Altered appetite	Feeling bad about self	Concentration problem	Psychomotor changes	Suicidal ideation
I feel sad.	.38**	.38**	.18	.09	.25*	.40***	.24*	.24*	.04
I feel irritable.	.33**	.30*	.15	.08	.20	.33**	.29*	.22	.04
I enjoy what I am doing.	.31*	.26*	.17	.09	.24*	.37**	.24*	.14	.00
I don't care about anything.	.37**	.31**	.03	.00	.18	.37**	.34**	.38**	.16
I have no appetite during the day.	.31**	.33**	.13	.12	.43***	.36**	.31**	.26*	.06
I worry about sleeping.	.21	.20	.57***	.34**	.31**	.28*	.19	.09	.13
I didn't have enough sleep last night.	.24*	.16	.32**	.38**	.19	.19	.21	.00	.08
I am restless.	.18	.24*	.28*	.13	.30*	.34**	.33**	.21	.13
I am tired.	.20	.13	.34**	.48***	.16	.25*	.14	.00	.00
It is not effortful to do things.	.21	.20	.40***	.38**	.21	.25*	.10	.10	.11
I am doing things with my normal pace.	.32**	.27*	.35**	.29*	.36**	.24*	.55***	.30*	.16
I feel worthless.	.33**	.43***	.22	.12	.36**	.55***	.39**	.26*	.23
I feel that I can't get anything done.	.40***	.38**	.26*	.20	.24*	.42***	.30*	.14	.17
I can't concentrate.	.38**	.34**	.35**	.32**	.30*	.42***	.37**	.10	.26*
I feel hopeless.	.41***	.52***	.25*	.17	.31**	.56***	.37**	.28*	.25*
How's your day?	.12	.33**	.13	.09	.29*	.31**	.20	.19	.05
How would you rate your overall physical health today?	.34**	.35**	.35**	.19	.45***	.35**	.38**	.14	.10

Note. Little interest = little interest or pleasure in doing things; feeling down = feeling down, depressed, or hopeless; trouble in sleep = trouble falling or staying asleep, or sleeping too much; tired = feeling tired or having little energy; altered appetite = poor appetite or overeating; feeling bad about self = feeling bad about yourself – or that you are a failure or have let yourself or your family down; concentration problem = trouble concentrating on things, such as reading the newspaper or watching television; psychomotor changes = moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual; suicidal ideation = thoughts that you would be better off dead of or hurting yourself in some way. * $p < .05$. ** $p < .01$. *** $p < .001$.

The discriminant and convergent validity of items measuring the same and different MD symptoms were also tested using Wilcoxon rank-sum test. We firstly calculated Spearman's rho between the mean momentary ratings over 14 days and the retrospective ratings measured after the participants completed all momentary assessments. Later, the calibrated *z* scores of the Spearman's rho were analyzed using the Wilcoxon rank-sum test. Consistent with the results of Study 1, the results supported the discriminant validity, which indicated the items measuring the same MD symptoms not only differed from but also converged more strongly across types of measurement than items measuring different symptoms (W = 1546.5, p = .003). This could be observed in the medians of the Spearman's rhos of the items measuring the same and different MD symptoms were .37 and .24, respectively. H1 was supported.

In order to test what type of momentary ratings best predicted retrospective ratings, we examined the peak-end rule by comparing the momentary and the retrospective ratings using the Wilcoxon signed rank test. Also, to test the peak-end rule more extensively, we not only compared the correlations between the retrospective ratings and the mean momentary ratings with the correlations between the retrospective ratings and the averages of the peak and the end momentary ratings but also the relationships between the retrospective ratings and the peak and the end momentary ratings. The same analyses as used in Study 1 were conducted on the same six pairs of comparisons. The peak momentary ratings represented the 75^{th} percentile of the momentary ratings, the end momentary ratings were calculated by averaging the momentary ratings of the last sampling day, and the peak-end momentary ratings were the means of the peak and the end momentary ratings. If one or some of the mean end momentary ratings were NAs, the mean momentary ratings of the previous sampling day were used until there was no NAs. For example, if there were NAs in one participant's mean momentary ratings of the last sampling day and the mean momentary ratings of the sampling day – Day 13 – of this participant were used. The results indicated significant differences between all the pairs except the mean momentary ratings and the peak

momentary ratings (p = .089). The significant pairs were the peak-end momentary ratings and the mean momentary ratings (V = 6597), the peak-end momentary ratings and the end momentary ratings (V = 8434), the mean momentary ratings and the end momentary ratings (V = 8503.5), and the peak momentary and the end momentary ratings (V = 7990.5, ps < .001). Table 2.6 shows the estimates and the p-values of the Wilcoxon signed rank tests and the medians of the Spearman's rhos. The medians of the Spearman's rhos of the mean momentary ratings (.25) and the peak momentary ratings (.25) were greater than that of the peak-end momentary ratings (.24). The median of the Spearman's rhos of the end momentary ratings was the smallest (.18). Consistent with Study 1, H2 was rejected.

Whether people rated their past MD symptoms less or more on their recent experiences were tested by comparing the mean momentary ratings of the first half of the sampling period (less recent) and the second half of the sampling period (more recent). The calibrated z scores of the Spearman's rhos between the retrospective ratings and the first half momentary ratings as well as those of the Spearman's rhos between the retrospective ratings and the second half momentary ratings were calculated separately. We then employed the Wilcoxon signed rank test to compare the calibrated z scores of the Spearman's rhos in pairs. Significant differences between the first half and the second half momentary ratings were found (W = 7484, p < .001). The medians of the Spearman's rhos between the retrospective ratings and the first half momentary ratings (.25) was greater than that between the retrospective ratings and the second half momentary ratings (.21). H3 was rejected. This was consistent with the results in Study 1.

We then explored the inter-correlations among the items measuring MD symptoms in the momentary and retrospective assessments using the PCA. The Spearman's rho of the retrospective ratings and the mean momentary ratings were used in the analysis. The loadings of the momentary and retrospective assessments ranged from .34 to .86 and from .52 to .80, respectively (Table 2.6). The first principal components of the retrospective explained 49 and those of the mean momentary assessments explained 44 percent of the total variance among the

variables, respectively. The medians of the momentary assessment and the retrospective assessment were .39 and .44, respectively. The results were inconsistent with those in Study 1, where the amount of variance explained by the mean momentary assessment was greater than those explained by the retrospective assessment. Regardless of the inconsistent results, the differences between the retrospective and momentary assessments were small and this indicated the momentary and retrospective assessments had similar item inter-correlations.

We also compared the item inter-correlations between the very first momentary ratings. The loadings ranged from -.01 to .88 and the first principal components only explained 26 percent of the total variance among the variables. The results demonstrated weak inter-correlations between the first momentary ratings, which was consistent with the results in Study 1 and confirmed the MD symptoms were highly variable and the momentary assessments could gauge these changes. The medians of the Spearman's rhos of the mean momentary ratings (.39), the retrospective ratings (.44), and the very first momentary ratings (.15) also illustrated similar results. H4 was supported.

Almost all results in Study 2 were consistent with those in Study 1. One minor exception arose when testing H4, the inter-correlations among the items in the retrospective assessment were greater than those among the items in the momentary assessment in this study, whereas the opposite was found in Study 1. However, these were merely minor differences and the inter-correlations were similar. As a replicate of Study 1, the results of this study increased the credibility of the results of Study 1. To further verify the results of Studies 1 and 2, Study 3 was conducted.

Study 3

Materials and Method

This was a replicate of Studies 1 and 2 with some minor modifications in the demographic and lifestyle questions and the DDI and the addition of a new

instrument – an activity sensor, Movisens EcgMove 3 (Movisens GmbH, Karlsruhe, Germany). The activity sensors collected data including heart rate, heart rate variability, numbers of steps participants took each day, activity classes, and energy expenditure. The data collected using the activity sensors will be used in Chapter 6.

Participants

Participants were recruited via e-mails through course organizers and department and school secretaries of the University of Edinburgh, posters in the campuses of the University of Edinburgh and in cafes and shops near the central campus, and social media. In total, 153 participants signed up for this study, 105 participants completed the initial questionnaire, and 78 participants provided valid and completed data (mean age = 25.46 and *SD* = 6.18). There were 57 female and 21 male participants.

Materials

One item was added to the demographic and lifestyle questions, - "What's the quality of your closest relationship?". This item had two anchoring points of "very good" and "very poor" on a 9-point Likert scale. In the DDI, two items were added, one item was modified and expanded into two items, two items were modified, and one item was replaced. The two added items are "What time did you go to bed last night?" and "What time did you wake up this morning?". The item “I feel sad” with two anchoring points of "happy" and "sad" was modified and extended into "I feel sad" and "I feel happy" and both items had anchoring points of "not at all" and "very much". “I feel that I don’t have enough sleep last night” was revised and became “I didn’t have enough sleep last night”. “I feel that I can’t get anything done” was revised into “I feel that I can’t make decisions” and the anchoring points were changed from “getting things done” and “not getting things done” to “can make decisions” and “cannot make decisions”. “It is not effortful to do things” was replaced by “I feel guilty” and the anchor points were revised from “effortful” and “effortless” to “guilty” and “not guilty”. Table A.5 in Appendix A shows the items and their corresponding anchoring points in the DDI used in Study 3.

Procedure

After participants signed up online and indicated the time they were available to collect an activity sensor from the researcher in the Department of Psychology, the University of Edinburgh, the researcher contacted and confirmed the collection time with the participants via e-mail. The researcher then explained the procedure of the study, helped the participants setting up their phones, and gave them an activity sensor. Different from Study 2, where participants using iOS devices completed all questionnaires on the mobile application, Qumi, in Study 3, all participants completed the retrospective questionnaires on Google Form and the momentary questionnaires on the applications – movisensXS for Android phone users and Qumi for iOS users. Participants were asked to complete five momentary questionnaires daily over a duration of 14 days and wore the activity sensors around their chests between the first and the last momentary questionnaires. After completing the study, the participants were asked to return the activity sensor to the Department of Psychology, the University of Edinburgh. The participants received a £8 monetary compensation and a report on the associations of the DDI items except the items only measured once a day, a report on heart rate and heart rate variability, and a report on daily physical activity.

The content of a heart rate and heart rate variability report included metabolic equivalent level, activity class (i.e., lying, sitting or standing, walking or active, jogging, and other), heart rate, heart rate variability spectrogram, low and high frequencies of heart rate variability spectrogram, the ratio of low and high frequency, and the Baevsky stress index, which is a measure of stress. Physical activity reports comprise activity class, hourly and daily breakdown of activity class, body position (i.e., lying supine, lying left, lying right, lying prone, upright, and other), number of steps participants took per day, and activity intensity.

Results

A total number of 4,297 valid momentary questionnaires from 78 participants were collected. The demographic statistics of the participants were

shown in Table 2.2. The reverse-scoring items were adjusted before further analyses. Table 2.8 shows the correlations between the mean momentary MD ratings (the DDI) and the retrospective MD ratings (the PHQ-9) in Spearman's rhos. All correlations were positive, which aligned with the results in Studies 1 and 2.

To test H1 of items measuring the same MD symptoms correlated greater than those measuring different MD symptoms, Wilcoxon rank-sum test was used. The Spearman's rhos between the mean momentary ratings and the retrospective ratings were transformed to *z* scores and were used in the Wilcoxon rank-sum test. The result showed significant differences between the two groups ($W = 1608$, $p = .005$). The medians of the Spearman's rhos measuring the same MD symptoms correlated greater than that of the Spearman's rhos measuring different MD symptoms (the same vs. different = .58 vs. .43). H1 was supported.

The peak-end rule was tested in H2 using Wilcoxon signed rank test. The same pairs of comparisons of the Spearman's rhos transformed *z* scores as in Studies 1 and 2 were analyzed. The mean momentary ratings and the peak-end momentary ratings correlated similarly with the retrospective ratings ($V = 5474$, $p = .547$, Table 2.6). However, the associations between the peak-end momentary ratings and the retrospective ratings were significantly different from those between the peak momentary ratings and the retrospective ratings ($V = 2911.5$, $p < .001$) and those between the end momentary ratings and the retrospective ratings ($V = 1790$, $p < .001$). The median of the Spearman's rhos revealed the peak-end momentary ratings (.42) were smaller than that of the mean momentary ratings (.44) but were larger than those of the peak (.41) and the end momentary ratings (.40). H2 was rejected.

Table 2.8 *Spearman's rhos between the PHQ-9 and DDI items in Study 3*

DDI item \ PHQ-9 item	Little interest	Feeling down	Trouble in sleep	Tired	Altered appetite	Feeling bad about self	Concentration problem	Psychomotor changes	Suicidal ideation
I feel happy.	.57***	.66***	.40***	.55***	.27*	.51***	.44***	.41***	.52***
I feel sad.	.48***	.60***	.49***	.56***	.32**	.55***	.48***	.51***	.53***
I feel irritable.	.31**	.40***	.31**	.44***	.32**	.31**	.46***	.25*	.33**
I enjoy what I am doing.	.57***	.58***	.45***	.57***	.33**	.46***	.44***	.40***	.55***
I don't care about anything.	.64***	.47***	.41***	.49***	.33**	.40***	.45***	.34**	.41***
I have no appetite during the day.	.41***	.45***	.38**	.45***	.28*	.45***	.37**	.43***	.43***
I worry about sleeping.	.16	.21	.36**	.39***	.00	.07	.25*	.09	.03
I didn't have enough sleep last night.	.18	.27*	.33**	.48***	.08	.12	.30**	.19	.28*
I am restless.	.21	.31**	.23*	.44***	.22	.40***	.37**	.27*	.38**
I am tired.	.24*	.33**	.29*	.54***	.11	.31**	.39***	.25*	.27*
I feel guilty.	.48***	.58***	.43***	.51***	.39***	.59***	.45***	.33**	.40***
I am doing things with my normal pace.	.22	.39***	.21	.28*	.29*	.35**	.24*	.34**	.23*
I feel worthless.	.45***	.60***	.48***	.62***	.40***	.66***	.52***	.46***	.57***
I feel that I can't make decisions.	.55***	.56***	.47***	.57***	.40***	.50***	.58***	.48***	.48***
I can't concentrate.	.52***	.54***	.45***	.62***	.43***	.50***	.60***	.42***	.45***
I feel hopeless.	.58***	.70***	.53***	.67***	.46***	.69***	.53***	.45***	.58***
How's your day?	.53***	.60***	.44***	.57***	.31**	.47***	.46***	.35**	.44***
How would you rate your overall physical health today?	.45***	.59***	.43***	.53***	.37**	.41***	.46***	.35**	.44***

Note. Little interest = little interest or pleasure in doing things; feeling down = feeling down, depressed, or hopeless; trouble in sleep = trouble falling or staying asleep, or sleeping too much; tired = feeling tired or having little energy; altered appetite = poor appetite or overeating; feeling bad about self = feeling bad about yourself – or that you are a failure or have let yourself or your family down; concentration problem = trouble concentrating on things, such as reading the newspaper or watching television; psychomotor changes = moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual; suicidal ideation = thoughts that you would be better off dead of or hurting yourself in some way. * $p < .05$. ** $p < .01$. *** $p < .001$.

H3 of recent experiences shaped people's memories was tested using Wilcoxon signed rank test. The first half and the second half momentary ratings were grouped according to the same criterion as used in Studies 1 and 2 – for each participant, the momentary ratings recorded before the median of all completed momentary ratings were in the group of the first half momentary ratings and the remains were the second half momentary ratings. Significant differences between the two groups were found ($V = 2836$, $p < .001$). The second half momentary ratings correlated greater with the retrospective rating than the first half momentary ratings as shown in the medians of the Spearman's rhos for the first half and second half momentary ratings was .39 and .44, respectively. H3 was supported, which was inconsistent with the results of Studies 1 and 2.

The inter-correlations between items in the momentary and retrospective assessments were analyzed using the PCA. The loadings ranged from .62 to .79 in the retrospective assessment and from .33 to .90 in the momentary assessment (Table 2.6). The first principal components of the retrospective assessment explained 53 percent of the variance and those of the momentary assessment explained 55 percent of the variance, which was consistent with the results in Study 1 but was inconsistent with those in Study 2, where the retrospective assessment explained more variance than the momentary assessment did. The medians of the Spearman's rhos of the momentary and the retrospective assessments were .51 and .47, respectively. This showed the items in the momentary assessment were highly correlated.

The high inter-correlations within the momentary assessment may be due to the same reason as described in Study 1 – their higher reliability. Therefore, the very first momentary ratings were analyzed using the PCA to examine this possibility. The loadings ranged from .29 to .73 and the first principal components explained 28 percent of the variance. The median of the Spearman's rhos of the very first momentary ratings was .22. The results showed no strong inter-correlations within the items in the momentary assessment and the items actually

varied hugely. H4 was supported, which was consistent with the results in Studies 1 and 2.

As a replicate of Studies 1 and 2, the results in Study 3 did generally confirmed the results in Studies 1 and 2. The only exception was H3 was rejected in Studies 1 and 2 but it was supported in Study 3.

Discussion

Items measuring the same MD symptoms in both the momentary and the retrospective assessments correlated stronger than those measuring different MD symptoms, which showed the same MD symptoms converged more comparing to different MD symptoms. This also demonstrated high internal consistency in items measuring the same MD symptoms in both assessments.

The peak-end rule was rejected in Studies 1, 2, and 3 but there were slightly differences. Mean momentary ratings consistently correlated more greatly with the retrospective ratings than the peak-end, the peak, and the end ratings in the three studies. The correlations between the peak-end ratings and the retrospective ratings were only greater than those between the end momentary ratings and the retrospective ratings in Studies 1 and 2 but the associations were larger than both the peak and the end momentary ratings in Study 3. The results showed when participants were asked to rate their MD symptoms retrospectively, they rated their feelings based on their average experiences. Across the three studies, the mean Spearman's rhos of the end momentary ratings correlated the least with the retrospective ratings, this may address a possible alternative explanation – the participants did not rate the retrospective assessments according to their end or more recent feelings (Broderick et al., 2008). In Studies 1 and 2, the comparison of the momentary ratings taken during the first half of the sampling period with those collected during the second half of the sampling period also demonstrated similar results, where people based their ratings of the retrospective assessment more on the first half than the second half of the sampling period. However, the results in Study 3 was the opposite – people rated their past experiences based on their

recent experiences, which showed end experiences of an event may influence how people gauged their previous experiences of the same event.

In three studies, the inter-correlations of the items in the retrospective and mean momentary assessments only differed slightly. But the inter-correlations of the very first momentary ratings were weak. This implied MD symptoms are highly variable and the momentary assessments could capture these changes. This finding may inspire some to reconsider the conventional view of MD as a coherent entity and the commonly used MD diagnostic criteria such as the total score in the DSM-V (Fried et al., 2014).

The results from three studies displayed similar patterns and illustrated replicable findings. Therefore, increasing the credibility of the findings. The small inter-correlations between the very first momentary ratings showed the MD symptoms are highly variable. Looking into the momentary changes in symptoms and viewing single symptoms separately instead of all symptoms listed in the diagnostic criteria collectively may be the way forward to bring in more light in understanding the heterogeneous nature of MD and developing possible treatment methods.

The associations between the retrospective and momentary assessments were analyzed in this chapter. In the next chapter, we examined the variability of MD symptoms and its relationships with demographic factors as possible moderators. These include age, gender, educational attainment, marital status, and employment status.

Chapter 3 Relationships between MD and the moderators

Introduction

Symptom variability and disorder severity

The diagnoses of psychiatric disorders are based on established diagnostic criteria. It has been argued, however, that symptoms fluctuate over time by being influenced by other time-varying factors. This may have crucial implications for the development of the disorders. Studying these variances might increase our understanding of psychiatric disorders (Hessler et al., 2013).

Seeing disorders as collections of ever-changing symptoms is consistent with the dynamic systems perspective on them. Viewing psychiatric disorders from the perspective of a nonlinear dynamical systems model rather than a static and linear systems model has gradually gained popularity in health science publications (Rickles et al., 2007). Originated from mathematics and physics, this model has a broad application in many disciplines (Castillo & Melin, 2003). In a nonlinear system, the state of the system develops as time passes and its initial state and the rules of how the system operates determine how the process unfolds (Rickles et al., 2007). Inputs are disproportional to outputs in nonlinear systems. Nonlinear systems include complex and chaotic systems. In complex systems, the behaviors between units within systems are diverse and collective. Chaotic systems are characterized by complicated, random, and sporadic behaviors. If systems are subject to the influences of their surroundings, these are open systems. In such systems, changes are influenced not only by the elements inside the systems but also by the elements outside the systems and the changes are time-dependent.

There have been many applications of dynamical systems model in studying psychiatric disorders (Hayes et al., 2007, 2015; Karp et al., 2004; Odgers et al., 2009). It was used to study the impact of psychotherapy on anxiety disorder, major depression (MD), personality disorder and substance abuse (Hayes et al., 2007), and therapeutic changes in MD (Hayes et al., 2015). Hayes et al. (2007) concluded the

changes brought about by psychotherapy were not linear and were discontinuous. Hayes et al. (2015) proposed a destabilization and transition model, where treatments destabilize the psychological system of an individual and then the system gradually transit to an improved state. A study on high risk violence associated frequent incidents of severe violence with symptom instability (Odgers et al., 2009). During maintenance treatments, higher symptom variability was linked to a greater possibility of future MD episodes but no difference between different treatment groups was reported (Karp et al., 2004). Items in the Hamilton depression scale displayed a range of variances between the participants in mean range of scores, possible range of scores, and mean range of scores divided by possible range of scores.

Seeing psychiatric disorders from the perspective of dynamical systems model, symptom fluctuations may be considered changes within systems, where each individual represents a system. Symptom variability and symptom stability might be used as indicators of symptom fluctuations. However, the two terms are usually deemed of sharing the same meaning but they are different and they describe different aspects of changes in symptoms (Ebner-Priemer et al., 2009). Variability describes "the dispersion of scores from a central tendency, does not consider the temporal order of scores (Ebner-Priemer et al., 2009, p. 196) while stability takes both dispersion and temporal order into account. Several MD related studies examined how symptom stability and symptom variability related to suicidal attempt and other psychiatric disorders (Dawood & Pincus, 2017; Melhem et al., 2019). Higher symptom instability and symptom variability of depressed mood and loss of interests and lower symptom instability and symptom variability in loss of interest were associated with pathological narcissism (Dawood & Pincus, 2017). Great MD severity and symptom variability were linked to high suicidal attempt (Melhem et al., 2019). We are curious about the relationship between MD symptom variability and MD severity. In this chapter, MD symptom variability was tested in three studies to assess the relationship between MD symptom variability and MD severity. It is hypothesised that MD severity is associated with MD symptom

variability: people with greater load of depressive symptoms do not just have more of them but also fluctuate in them more. In addition to testing the direct links between MD severity, assessed with a one-off questionnaire, and symptom variability over time and across situations, we linked known correlates of depression severity with the variability in symptoms.

Age and MD

MD patient's age of onset rather than their current age was related with MD morbidity, especially in those who had an early age of onset (Coryell et al., 2009). Studying the age of onset in mental disorders is difficult because the mostly used measurements are patients' retrospective self-reports, where objective evidences are often missing due to the lengthy gaps between disorder onset and the first treatment (Angold et al., 1996; Kessler et al., 2007). Although no consensus has been reached regarding the cut-off age of late-onset MD or whether age of onset could be used to distinguish MD subgroups, the results from many studies have shown early- and late-onset MD are clinically different (Variend & Gopal, 2008). Late-onset MD related more with physical illnesses, structural changes in the brain, and cognitive deficits. Early-onset MD patients usually have personality disorders, are more neurotic, and encounter less of stressful life events than those with late-onset MD (Bukh et al., 2011). It was not clear whether the treatment outcomes for early- or late-onset MD was better than the other because there were reports of similar level of treatment outcome (Bukh et al., 2011) as well as late-onset MD being harder to treat (Variend & Gopal, 2008). Controversial results were also found in MD relapse in those having early- or late-onset MD. However, starting treatment early had been reported as playing a pivotal role in the progression of MD. In a review, de Girolamo, Dagani, Purcell, Cocchi, and McGorry (2012) emphasized the crucial role of early discovery and early intervention to treat MD at an early stage. The benefits of early treatment included stopping the symptoms from becoming more serious and preventing MD patients from having other comorbid disorders. Extrapolating from research pertaining to MD severity, this study tested the effect

of chronological age had on MD symptom variability. We hypothesize age would not have any effect on MD symptom variability.

Sex difference in MD

There have been consistent reports on greater number of female MD patients than male patients (M. Weissman & Olfson, 1995). Gender biases within family may be one of the possible explanations because family members tended to attribute mental problems of females in a family as caused by MD and suggested them to seek clinical diagnosis and treatment (Brommelhoff et al., 2004). This may result in over-reporting in females. Also, gender bias in MD diagnosis may be another potential cause of the uneven number between female and male patients. In addition, both direct and indirect relationships between MD and gender may contribute to this disparity (Bertakis et al., 2001). The indirect association was mediated through medical use rate. Compared to males, females use medical services more frequently, which may explain why more females were diagnosed with MD. However, recurrent clinic visits were associated with incorrect and correct MD diagnoses. For both men and women, no matter what they scored on the Beck Depression Inventory (BDI), they were more likely to be diagnosed with MD if they visited clinics more often. Females with a high BDI score were more likely to be diagnosed with MD than their male counterparts. These potentially incorrect diagnoses may result in an imbalance in medical resource distribution – those who need medical services could not receive suitable treatments because most of the resources were occupied by those who might not need them. Bertakis et al. (2001) also reported MD diagnosis was associated with educational attainment and marital status in women. Females were also more seriously affected by challenging changes in life, which caused those who have already being diagnosed with MD to develop more serious MD symptoms or those who had recovered from MD or had never had MD previously to receive MD diagnosis (Lorant et al., 2007).

Interestingly, when the MD symptoms listed in the DSM and the alternative "male-type" MD symptoms were both assessed, the imbalanced gender ratio in MD patients disappeared (Martin et al., 2013). Previous studies have reported men and

women experienced different depressive symptoms (Addis, 2008; Lynch & Kilmartin, 2013; Rutz, 1999; Rutz et al., 1995). Women usually have more internal emotion problems and sleep problems. Men have more external symptoms such as anger, substance abuse, womanizing, workaholism, gambling, feeling irritable, and aggressive behaviors. Although some studies reported no sex differences in the male-type symptoms, "qualitative gender-related differences" of greater inter-correlations between these symptoms were found in men but not in women (Möller-Leimkühler et al., 2004, p. 90). Therefore, including the measures of male-type MD symptoms may explain more variances in MD patients or participants of MD studies (Martin et al., 2013). Sex differences in MD has been studied in several aspects including stress responses (Bale & Epperson, 2015), pathways causing MD (Kendler & Gardner, 2014), and the influences of sex hormones (Altemus et al., 2014). Extrapolating from this research, we explore whether MD symptom variability was more prominent in females than in males.

Educational attainment and MD

Although there have been reports supporting that educational attainment was negatively related to MD, the association was not firmly established because both positive and negative associations were found. In a cross-nation study of 18 countries, significant negative relationships between educational attainment and MD were found in two out of the ten high-income (Israel and the USA) and three out of the eight low- to middle-income countries (India, Mexico and Ukraine) (Bromet et al., 2011). But significant positive relationships were also observed in one high-income (Japan) and one low- to middle-income country (China). One possible explanation of why MD associated negatively with educational attainment was having an early onset of psychiatric disorders including MD may disrupt learning and resulted in low educational attainment (Berndt et al., 2000; Kessler et al., 1995).

A multinational study of seven countries reported that comorbidities of anxiety disorders, mood disorders and substance-use disorders were more common in people with low educational attainment in six countries (World Health

Organization, 2000). However, the reverse association – high educational attainment and low comorbidity rate was not reported. Studies on the genetic correlation between educational attainment and MD showed both negative (Boardman et al., 2015; López-León et al., 2009) and positive associations (Mezuk et al., 2008; Peyrot et al., 2015). Low childhood intelligence was associated with higher chances of psychological stresses including anxiety and MD (Gale et al., 2009). High intelligence was linked to great educational attainment in England (Deary et al., 2007). Therefore, a negative association may exist between intelligence and MD via educational attainment.

Environmental influencers such as socioeconomic status (SES) may be the primary contributor of the association between educational attainment and MD (Peyrot et al., 2015). A meta-analysis study of 51 studies and six countries used educational attainment, income, and occupation, social class and other measures of SES (Lorant et al., 2003). The authors observed a negative relationship between educational attainment and MD onset as well as MD persistence. However, using educational attainment as one of the typical assessments of SES (Oakes & Rossi, 2003), may complicate the disentanglement of the influences of educational attainment and other SES measurements on MD. To test the relationship between educational attainment and MD symptom variability, we hypothesize that people with low educational attainment would have greater MD symptom variability than those with high educational attainment.

Marital status and MD

There have been consistent findings of higher MD prevalence in those who were unmarried, widowed, or divorced than those who were married (Andrade et al., 2003). Varied associations were found in low- to middle-income and high-income countries: in high-income countries, MD was associated with being separated or never married while in low- and middle-income countries, being

divorced or widowed were related to MD (Bromet et al., 2011). Ending cohabitation also increased MD severity and the odds of MD diagnoses in women (Lorant et al., 2007). Nevertheless, the causality between MD and marital status was not clear because psychiatric disorders was linked to a low marriage stability – high divorce rate and short years of marriage (Kessler et al., 1998). Contrasting likelihoods of being diagnosed with MD were observed in different union types (S. L. Brown, 2000). Cohabiting couples had a higher probability of being diagnosed with MD than married couples. This may be caused by higher level of relationship instability experienced among cohabiting couples than in married couples. Nonetheless, Perelli-Harris and Styrc (2017) suggested childhood selection might be a determinant factor of the mental well-being in married and cohabiting couples. They argued childhood selection, which was shaped by parental influences and was formed during childhood, caused people to choose whether to marry or cohabit. To test the relationship between marital status and MD symptom variability, we hypothesize those who were not married would have greater MD symptom variability than those who were married.

Employment status and MD

The link between employment status and mental health drew people's attention particularly during economic recession. A review suggested a highly possible association between economic recession and mental health in Europe and North America (Frasquilho et al., 2016). The numbers of people having mental health problems, using substances, having suicidal behaviors, and deteriorated well-being after recessions were greater than these prior to recessions. Vulnerable groups including those who were old, unemployed, indebted, or facing financial hardships, had insecure jobs, and had families and children. Despite the effect of parental unemployment on the mental health of children and young people being indirect, it may have lasting consequences even after these children and young people have entered adulthood.

The health benefits of employment on MD and psychological stress were highlighted in a review paper, which analyzed longitudinal studies on employment

or reemployment and health outcome (van der Noordt et al., 2014). Due to a lack of consistent evidence, whether employment had any effect on general health, physical health, and mortality was unclear. But being employed did protected people from having MD. Several studies have reported unemployment was positively correlated with depression in many countries including Portugal (Rodrigues et al., 2017), Greece, and Spain (Gili et al., 2013; Iglesias Garcia et al., 2014).

Other dimensions of work and aspects of the workplace may influence the mental health of jobholders. These include job authority, job demand, and social support, task variation, and learning opportunity. The Demand-Control model demonstrated a combination of high job demand and low level of control over one's job would cause mental stress (Karasek, 1979). A later expansion of this model – the Demand-Control-Support model – assumed social support among colleagues at work would enhance workers' capacity to handle stress (J. V. Johnson & Hall, 1988). Vanroelen, Levecque, and Louckx (2009) examined these two models and found employees' mental health was mainly affected by job demand and social support. We test how employment status linked to MD symptom variability with a hypothesis of employment status correlates with MD symptom variability – those who are unemployed had higher level of MD symptom variability then those who are employed.

The studies

The relationships between the moderators discussed above and the variabilities of MD symptoms are tested in three studies and the following six hypotheses are tested. We also explore whether MD is a homogeneity or heterogeneity entity in these relationships. We expect that if depression is a heterogeneous entity, this would reflect in the ways different symptoms relate to MD severity and assorted fluctuations would be observed.

H5: High variability in momentary ratings reflects MD severity as defined by retrospective ratings; after all, mood variability is a definitional symptom of MD. More frequent and a greater magnitude differences in momentary ratings should

correspond with high scores in the retrospective MD symptom ratings – the Patient Health Questionnaire 9 (PHQ-9) – completed after the momentary assessments. The influences of age, gender, educational attainment, marital status, and employment status on MD severity are also tested. For example, it could be that people with different levels of education vary in how their MD symptoms fluctuate. H6: Chronological age has no effect on MD symptom variability. H7: MD symptom variability is more prominent in females than in males. H8: People with low educational attainment would have greater MD symptom variability than those with high educational attainment. H9: Those who were married have less MD symptom variability than those who were not married. H10: Employment status correlates with MD symptom variability such that unemployed have higher level of MD symptom variability then those who are employed. All *p*-values were corrected using false discovery rate.

Materials and Method

The materials, procedure, and participants were the same as described in Studies 1, 2, and 3 in Chapter 2. Kroenke, Spitzer, and Williams (2001) reported a PHQ-9 score 10 or larger had a sensitivity of 88%, a specificity of 88%, and a positive likelihood ratio of 7.1 in diagnosing MD. Here, a PHQ-9 score of 10 or larger was used as a cut-off point to determine MD severity.

Results

Study 1

Standard deviation (SD) of each item in the Daily Depression Items (DDI) were used as an indicator for symptom variabilities (Table 3.1). The minimum and maximum SDs among the participants were listed in Table 3.1. The differences between the minimum and maximum SDs in the overall SDs ranged from 21.93 (for the item "*I don't care about anything*") to 30.96 (for the item "*I feel that I didn't have enough sleep last night*").

The associations between MD severity, age, gender, educational attainment, marital status, and employment status and the variability of each item in the DDI were tested using a linear model. The R code of this model was listed in Appendix B. In linear models, variability of each item in the DDI was the dependent variable (DV) and PHQ-9 score, age, gender, marital status, educational attainment, and employment status were the independent variables (IVs). Among the IVs, age and educational attainment were continuous and gender, marital status, and employment status were categorical. Educational attainment was treated as a continuous variable because the levels were in a chronological order Employment status had six levels and marital status was consisted of five levels. Considering treating these two variables as factors may cause collinearity issues or undermine power, therefore, they were collapsed into fewer levels. Employment status was collapsed into two groups, where employed or self-employed and full-time student were in one group and part-time employed, retired, and unemployed were in another group. Marital status was collapsed into two levels where single, divorced, and widowed were collapsed into one group and in a relationship and married were in another group.

In addition, five participants provided answers for their employment status other than the provided options, so their answers to this question were re-categorized to fit into the five existing options and then into the two groups described above. These were one participant identified himself/herself as an underemployed freelancer in the part-time employed group, two participants identified himself/herself as a student and one participant regarded himself/herself as paid to be a full-time PhD student in the full-time student group, and one participant who claimed that he/she will be employed in the near future in the unemployed group.

Table 3.1 *SDs of the DDI items in Studies 1, 2, and 3*

DDI item	*Overall SD*			Minimum SD			*Maximum SD*		
	Study 1	Study 2	Study 3	Study 1	Study 2	Study 3	Study 1	Study 2	Study 3
I feel happy.	-	-	22.06	-	-	0	-	-	32.29
I feel sad.	21.97	21.35	23.60	2.53	1.25	0	34.76	29.20	29.45
I feel irritable.	23.56	21.67	24.28	2.35	.79	0	34.09	31.99	35.08
I enjoy what I am doing.	23.05	21.87	23.73	2.10	.64	5.17	36.37	34.91	34.88
I don't care about anything.	21.93	20.72	25.80	2.27	3.30	0	35.89	32.67	40.19
I have no appetite during the day.	24.75	22.50	22.70	.77	0	0	46.06	40.44	43.59
I worry about sleeping.	30.19	28.05	28.78	2.22	2.00	0	49.94	65.76	47.38
I didn't have enough sleep last night.	30.96	28.98	30.62	1.73	3.56	0	45.89	43.40	48.34
I am restless.	26.65	24.03	26.65	1.97	0	4.47	39.47	32.28	36.81
I am tired.	29.40	26.94	28.55	1.99	2.42	5.22	40.78	35.28	39.95
It is not effortful to do things.	26.78	25.45	-	1.46	6.48	-	39.44	36.35	-
I feel guilty.	-	-	30.38	-	-	0	-	-	37.55
I am doing things with my normal pace.	-	11.93	12.11	-	0	0	-	23.22	20.27
I feel worthless.	24.92	22.80	26.71	1.87	0	0	33.56	28.99	32.11
I feel that I can't get anything done.	27.73	23.06	-	2.18	5.52	-	39.07	31.73	-
I feel that I can’t make decisions.	-	-	24.56	-	-	0	-	-	30.99
I can't concentrate.	27.12	22.85	26.60	2.10	3.58	1.13	35.70	33.52	33.68
I feel hopeless.	24.40	22.65	26.30	2.14	2.98	0	35.17	29.20	40.09
How's your day?	24.04	22.38	23.02	2.46	2.52	4.16	39.13	43.41	35.60
How would you rate your overall physical health today?	-	23.41	25.54	-	4.93	0	-	40.31	49.50

Note. Overall SD is the SD for the rating provided by all participants for each item in the DDI. Minimum and maximum SDs are the minimum and maximum SDs for each item in the DDI among individual participants.

Among all models, MD severity was a significant predictor of the variabilities of more than half items in the DDI - "*I feel sad*", "*I enjoy what I am doing*", "*I don't care about anything*", "*I have no appetite during the day*", "*I am restless*", "*I feel worthless*", "*I feel hopeless*", and "*How's your day*" (Table 3.2). Frequent fluctuations in MD symptoms thus reflected MD severity and H5 was partially supported. MD severity did not significantly predict the variability of all DDI items suggested MD is heterogeneous. Age did not significantly predict the variability of any DDI items and H6 was therefore supported (Table 3.3). Since gender, educational attainment, marital status, and employment status were not significant predictors of MD severity, H7, H8, H9, and H10 were rejected. The moderators related to the variability of MD symptoms similarly and thus supporting MD homogeneity but the matching demographics of the participants might be the cause. The standardized betas and *p*-values of age, gender, educational attainment, marital status, and employment status for each DDI item were shown in Tables 3.3–3.7. Figures showing the patterns of the standardized betas of the moderators were listed in Appendix C, where matching patterns could be observed for most items in PHQ-9 score and but not for age, gender, educational attainment, marital status and employment status.

Table 3.2 *Standardized betas and p-values of PHQ-9 score from regression models testing the variabilities of the DDI items in Studies 1, 2, and 3*

DDI item	*β*			*p*		
	Study 1	Study 2	Study 3	Study 1	Study 2	Study 3
I feel happy.	-	-	.05	-	-	.899
I feel sad.	.34	.19	.03	.010	.405	.951
I feel irritable.	.23	.19	.12	.133	.293	.637
I enjoy what I am doing.	.34	.09	.04	.008	.813	.899
I don't care about anything.	.35	.32	.37	.006	.088	.027
I have no appetite during the day.	.33	.31	.25	.014	.163	.255
I worry about sleeping.	.11	.07	.10	.640	.878	.790
I didn't have enough sleep last night.	.14	.15	-.07	.494	.461	.881
I am restless.	.28	.15	.06	.043	.332	.887
I am tired.	-.12	-.04	-.10	.619	.998	.812
It is not effortful to do things.	-.12	.03	-	.629	.829	-
I feel guilty.	-	-	.13	-	-	.692
I am doing things with my normal pace.	-	.41	.27	-	.016	.183
I feel worthless.	.42	.28	.26	< .001	.142	.227
I feel that I can't get anything done.	.23	.19	-	.133	.326	-
I feel that I can’t make decisions.	-	-	.27	-	-	.127
I can't concentrate.	.25	.24	.04	.091	.255	.939
I feel hopeless.	.39	.27	.17	.001	.142	.483
How's your day?	.30	.14	.05	.020	.812	.905
How would you rate your overall physical health today?	-	.34	-.02	-	.252	.955

Table 3.3 *Standardized betas and p-values of age from regression models testing the variabilities of the DDI items in Studies 1, 2, and 3*

DDI item	*β*			*p*		
	Study 1	Study 2	Study 3	Study 1	Study 2	Study 3
I feel happy.	-	-	-.26	-	-	.277
I feel sad.	-.11	.03	-.23	.640	.951	.405
I feel irritable.	-.18	.02	.02	.332	.960	.960
I enjoy what I am doing.	-.23	-.04	-.34	.152	.943	.098
I don't care about anything.	-.17	.08	-.25	.328	.878	.255
I have no appetite during the day.	-.06	-.24	-.28	.828	.405	.252
I worry about sleeping.	-.07	.16	-.21	.822	.657	.405
I didn't have enough sleep last night.	-.07	.06	-.03	.825	.905	.943
I am restless.	-.16	.01	-.22	.417	.979	.405
I am tired.	-.07	.14	-.01	.822	.676	.990
It is not effortful to do things.	-.13	-.11	-	.619	.816	-
I feel guilty.	-	-	-.26	-	-	.260
I am doing things with my normal pace.	-	.04	-.30	-	.943	.189
I feel worthless.	-.12	-.15	-.21	.571	.698	.405
I feel that I can't get anything done.	-.25	.00	-	.127	1.000	-
I feel that I can’t make decisions.	-	-	-.26	-	-	.203
I can't concentrate.	-.24	.10	-.20	.147	.822	.467
I feel hopeless.	-.18	.03	-.41	.259	.960	.027
How's your day?	-.19	.10	-.24	.282	.816	.322
How would you rate your overall physical health today?	-	.07	-.25	-	.881	.293

Table 3.4 *Standardized betas and p-values of gender from regression models testing the variabilities of the DDI items in Studies 1, 2, and 3*

DDI item	*β*			*p*		
	Study 1	Study 2	Study 3	Study 1	Study 2	Study 3
I feel happy.	-	-	-.27	-	-	.678
I feel sad.	-.22	-.47	-.18	.678	.373	.816
I feel irritable.	-.27	-.12	-.18	.578	.892	.817
I enjoy what I am doing.	-.07	-.57	-.22	.905	.255	.714
I don't care about anything.	-.05	-.27	-.16	.943	.714	.817
I have no appetite during the day.	-.02	-.18	-.10	.980	.822	.899
I worry about sleeping.	.27	.02	-.51	.624	.986	.255
I didn't have enough sleep last night.	.08	-.39	-.28	.899	.571	.676
I am restless.	.00	-.32	-.24	1.000	.655	.728
I am tired.	.24	-.87	-.24	.657	.020	.731
It is not effortful to do things.	-.10	-.56	-	.892	.293	-
I feel guilty.	-	-	.04	-	-	.960
I am doing things with my normal pace.	-	.21	.13	-	.810	.878
I feel worthless.	.00	-.04	-.04	1.000	.960	.960
I feel that I can't get anything done.	-.16	-.66	-	.800	.158	-
I feel that I can’t make decisions.	-	-	-.43	-	-	.255
I can't concentrate.	-.21	-.66	-.51	.696	.203	.255
I feel hopeless.	-.32	-.24	.10	.405	.788	.897
How's your day?	-.03	-.08	-.34	.960	.943	.527
How would you rate your overall physical health today?	-	-.36	-.42	-	.570	.398

Table 3.5 *Standardized betas and p-values of educational attainment from regression models testing the variabilities of the DDI items in Studies 1, 2, and 3*

DDI item	*β*			*p*		
	Study 1	Study 2	Study 3	Study 1	Study 2	Study 3
I feel happy.	-	-	-.03	-	-	.943
I feel sad.	.08	.03	.11	.764	.943	.787
I feel irritable.	.08	.10	-.25	.764	.816	.255
I enjoy what I am doing.	.01	.14	-.17	.964	.699	.461
I don't care about anything.	-.02	.11	.01	.945	.813	.986
I have no appetite during the day.	.04	.17	.24	.899	.640	.255
I worry about sleeping.	-.03	-.03	-.11	.943	.943	.751
I didn't have enough sleep last night.	-.01	-.15	-.12	.960	.721	.714
I am restless.	.12	-.12	-.06	.578	.787	.884
I am tired.	-.08	-.15	-.19	.787	.640	.475
It is not effortful to do things.	.02	-.01	-	.951	.990	-
I feel guilty.	-	-	.05	-	-	.892
I am doing things with my normal pace.	-	-.02	-.01	-	.966	.979
I feel worthless.	.00	.10	.22	.990	.822	.319
I feel that I can't get anything done.	-.11	-.07	-	.619	.884	-
I feel that I can’t make decisions.	-	-	-.08	-	-	.812
I can't concentrate.	.02	-.08	-.19	.943	.873	.417
I feel hopeless.	.04	.02	.24	.884	.966	.253
How's your day?	.07	.00	-.08	.812	.990	.817
How would you rate your overall physical health today?	-	-.06	-.18	-	.899	.482

Table 3.6 *Standardized betas and p-values of marital status from regression models testing the variabilities of the DDI items in Studies 1, 2, and 3*

DDI item	*β*			*p*		
	Study 1	Study 2	Study 3	Study 1	Study 2	Study 3
I feel happy.	-	-	.19	-	-	.816
I feel sad.	-.01	-.09	.07	.990	.939	.943
I feel irritable.	.07	-.19	.13	.908	.822	.884
I enjoy what I am doing.	-.01	.01	.44	.986	.990	.331
I don't care about anything.	-.27	-.08	-.05	.445	.943	.951
I have no appetite during the day.	-.04	-.16	.03	.959	.881	.964
I worry about sleeping.	-.10	-.11	-.12	.878	.905	.884
I didn't have enough sleep last night.	.07	-.32	.04	.899	.699	.964
I am restless.	.01	-.29	.20	.990	.710	.810
I am tired.	.00	-.19	.28	.990	.817	.687
It is not effortful to do things.	-.14	-.12	-	.813	.905	-
I feel guilty.	-	-	.01	-	-	.990
I am doing things with my normal pace.	-	-.34	.06	-	.657	.943
I feel worthless.	.06	-.36	-.13	.920	.657	.884
I feel that I can't get anything done.	-.12	-.28	-	.816	.701	-
I feel that I can’t make decisions.	-	-	-.32	-	-	.497
I can't concentrate.	-.07	-.34	-.27	.897	.667	.676
I feel hopeless.	-.11	-.14	-.09	.822	.891	.899
How's your day?	.06	.20	-.19	.939	.822	.810
How would you rate your overall physical health today?	-	-.40	-.06	-	.571	.943

Table 3.7 *Standardized betas and p-values of employment status from regression models testing the variabilities of the DDI items in Studies 1, 2, and 3*

DDI item	*β*			*p*		
	Study 1	Study 2	Study 3	Study 1	Study 2	Study 3
I feel happy.	-	-	.26	-	-	.816
I feel sad.	-.11	-.20	.16	.878	.822	.894
I feel irritable.	-.17	-.05	-.18	.788	.960	.884
I enjoy what I am doing.	-.18	-.35	.49	.737	.640	.483
I don't care about anything.	-.10	-.41	.21	.881	.570	.825
I have no appetite during the day.	.04	-.08	.23	.955	.943	.822
I worry about sleeping.	-.25	-.01	.18	.653	.990	.884
I didn't have enough sleep last night.	.15	-.19	.53	.816	.850	.505
I am restless.	-.11	-.12	.15	.873	.899	.897
I am tired.	-.32	-.58	.17	.475	.252	.887
It is not effortful to do things.	-.15	-.10	-	.816	.939	-
I feel guilty.	-	-	.70	-	-	.279
I am doing things with my normal pace.	-	-.34	.34	-	.660	.696
I feel worthless.	-.22	-.17	.57	.657	.878	.405
I feel that I can't get anything done.	-.14	-.32	-	.816	.660	-
I feel that I can’t make decisions.	-	-	.70	-	-	.203
I can't concentrate.	-.05	-.27	.05	.943	.756	.960
I feel hopeless.	-.11	-.32	.33	.845	.699	.710
How's your day?	-.06	-.35	.57	.943	.657	.415
How would you rate your overall physical health today?	-	-.19	.16	-	.822	.887

The inter-correlations of the variabilities of the items were tested using the PCA; this was to see whether within-individual variability was a common property across depressive symptoms with those varying more in one also tending to vary more in others; if not, this would be consistent with the symptoms being heterogeneous. The results illustrated the variabilities of some DDI items were indeed highly correlated, with their loadings on the first principal component ranging from .47 to .86 and the first principal component explaining 54 percent of

the total variance among the item variabilities (Table 3.8). The symptom variations exhibited similar patterns, which supported the view of a single cause underlying all MD symptoms. However, the range of loadings may imply great differences exist in the variances explained by the single underlying cause.

The sample consisted mainly of female undergraduate students. This may explain why none of the moderators were significant predictors of MD symptom variability. Two more studies were conducted to further test the hypotheses.

Table 3.8 *PCA loadings of the variabilities of the DDI items in Studies 1, 2, and 3*

DDI item	Study 1	Study 2	Study 3
I feel happy.	-	-	.77
I feel sad.	.83	.70	.69
I feel irritable.	.84	.72	.67
I enjoy what I am doing.	.83	.74	.73
I don't care about anything.	.76	.61	.66
I have no appetite during the day.	.58	.39	.52
I worry about sleeping.	.51	.43	.39
I didn't have enough sleep last night.	.64	.61	.41
I am restless.	.78	.72	.68
I am tired.	.47	.62	.62
It is not effortful to do things.	.53	.73	-
I feel guilty.	-	-	.70
I am doing things with my normal pace.	-	.67	.59
I feel worthless.	.79	.69	.67
I feel that I can't get anything done.	.85	.84	-
I feel that I can’t make decisions.	-	-	.72
I can't concentrate.	.86	.85	.79
I feel hopeless.	.85	.80	.73
How's your day?	.75	.55	.72
How would you rate your overall physical health today?	-	.45	.47
Total variance explained	54%	45%	42%

Study 2

Symptom variabilities for each item in the DDI were represented as within individual, over time SDs of each item. The minimum and the maximum SDs among all participants and the group SDs were listed in Table 3.1. The differences between minimum and maximum SDs in the overall SDs ranged from 20.72 (“*I don’t care*

about anything") to 29.98 (for the item "*I feel that I didn't have enough sleep last night*").

The same regression model as used in Study 1 was used here. PHQ-9 score significantly predicted the variability of "*I am doing things with my normal pace*" (Table 3.2). H5 was thus only vaguely supported. This corresponded with Study 1, where MD severity only significantly predicted the variability of some DDI items and suggested MD heterogeneity. Since none of the moderators significantly predicted the variability of MD symptoms except gender, H6 was supported (Table 3.3) and H7 was marginally supported (Table 3.4). H8 – H10 were rejected (Tables 3.5–3.7). H7 was only marginally supported because one item – feeling tired – was significantly predicted by gender and greater variability in women than in men was found (β = -.87, p = .019). The similar patterns of insignificance across moderators and MD symptom variability could be interpreted as supporting MD symptom homogeneity but the same as in Study 1, the matching demographics of the participants might be a plausible explanation instead. The incongruent results with those in Study 1 were H5 and H7 were marginally supported. The number of participants in Study 2 was smaller than that in Study 1 and this might explain the fewer significant associations between MD severity and symptom variabilities.

The PCA was employed to test the inter-correlations of the variability of the DDI items. The loadings spread over a broad range between .39 and .85 and the total variance explained by the first principal component was 45 percent, which was smaller than that in Study 1 (Table 3.8). The wider range of PCA loadings and the total variance explained by the first component might illustrate greater variabilities among the DDI symptoms and within-individual variability might be a less common characteristic among MD symptoms; of course, this may have resulted from the smaller sample size. Therefore, one more study was conducted to exam the findings in Studies 1 and 2.

Study 3

The variabilities of the DDI items were SDs as shown in Table 3.1. The maximum and minimum SDs among participants were listed in Table 3.1 as well. The differences between the maximum and the minimum SDs in the overall SDs spanned across 22.06 (for the item "*I feel happy*") and 30.62 (for the item "*I didn't have enough sleep last night*").

PHQ-9 score significantly predicted the variability of "*I don't care about anything*". H5 was only vaguely supported (Table 3.2). This showed varied pattern of associations between MD severity and symptom variability and suggested MD symptom heterogeneity. Chronological age was a significant predictor of the variability of "*I feel hopeless*" and H6 of chronological age had no effect on MD symptom variability was marginally rejected (Table 3.3). None of other moderators including sex, educational attainment, marital status, and employment status significantly predicted the variabilities of any DDI items and H7 – H10 were rejected (Tables 3.4–3.7). These similar insignificant patterns in the moderators supported homogeneity in MD symptoms but the homogeneity in participant demographics may contribute greatly to these patterns. The results were similar to those in Studies 1 and 2 except H6 was marginally rejected but it was supported in Studies 1 and 2. H7 was rejected in Studies 1 and 3 but it was vaguely supported in Study 2.

Inter-correlations of DDI item variabilities were tested using the PCA. The range of loadings was .39 – .79, which was smaller than Study 2 but greater than Study 1 (Table 3.8). The first principal component explained a total variance of 42%, which was the smallest in the three studies, but it still fell in a similar range and suggested similar inter-correlations in MD symptom variabilities.

Replicability across Studies 1, 2 and 3

To test the replicability of the results of the relationship between MD symptom variability and MD severity and other moderators replicated across the three studies, we compared the standardized betas linking DDI items to PHQ-9 scores, age, gender, educational attainment, marital status, and employment status;

the similarities of the respective vectors of betas were estimated using Spearman rank-order correlation. Tables 3.2–3.7 (and the Appendix C) show the standardized betas and *p* values of these variables in the three studies.

The correlation coefficients revealed that only MD severity and MD symptom variability replicated across the three studies. The results of PHQ-9 score demonstrated Studies 1 and 2 (r = .72) and Studies 2 and 3 (r = .73) were highly correlated and Studies 1 and 3 (r = .59) were moderately associated (Table 3.9). Most of the correlations between MD severity and other moderators including age, gender, educational attainment, marital status, and employment status were either small, moderate, or even negative. This was expected, given that the effects were generally small and thereby largely reflected noise; this means that the inconsistent correlations of betas across studies could also be seen as confirming lack of overall effects. Therefore, the results of other moderators were unreproducible. The Tucker's congruence coefficients between PCA loadings of the three studies (φs = .99) demonstrated the factors in the three studies could be considered equal (Lorenzo-Seva & Berge, 2006), meaning symptom variabilities are highly inter-correlated but the differences between symptoms in the degrees of reflecting a general variance factor were consistent (Table 3.9). On the on hand, this supported the view of MD symptoms are homogeneous (as their variabilities were inter-correlated). On the other hand, this supports symptoms having their own etiology as their variabilities were systematically variable in coalescing around a single factor.

Table 3.9 *Spearman's rho of the standardized betas for PHQ-9 score, age, gender, educational attainment, marital status, and employment status between the studies*

Variables	*r*		
	Study 1 vs. Study 2	Study 1 vs. Study 3	Study 2 vs. Study 3
PHQ-9 score	.72	.59	.73
Age	.02	.20	.32
Gender	.19	-.42	.36
Educational attainment	.25	.19	.46
Marital status	-.31	.25	.13
Employment status	-.04	.13	-.30

Note. *r* = Spearman's rho.

Meta-analysis

Finally, we sought to meta-analyses the findings across the three studies: individually, each of them may have been underpowered, but collectively they would yield more powerful and generalizable findings. The sample size of each study and the standardized betas and standard errors of PHQ-9 score, age, gender, educational attainment, marital status, and employment status from the regression models were used in the meta-analysis. The results of the variables diverged greatly. Nominally, PHQ-9 score had significant associations with the within-individual variabilities in 12 DDI items; after applying FDR to correct for multiple testing, five associations remained significant at the adjusted alpha = .0025 level; "*I don't care about anything*", "*I have no appetite during the day*", "*I am doing things at my normal pace*", "*I feel worthless*", and "*I feel hopeless*" (Table 3.10). Some meta-analytic effects were small or even negative, consistent with the symptoms differentially reflecting the degree of MD severity. Other moderator-candidates either only had significant effects on a few or none of the DDI items (Tables 3.11–3.15). Age and gender had two and one significant associations, respectively.

Table 3.10 *Meta-analysis of standardized betas of PHQ-9 predicting DDI item variability in the three studies* (*N* = 277)

DDI item	*β*	*SE*	*Z*	*p*
I feel happy.	.05	.12	.42	.897
I feel sad.	.23	.06	3.63	.011
I feel irritable.	.21	.06	3.38	.020
I enjoy what I am doing.	.19	.06	3.10	.035
I don't care about anything.	.36	.06	5.91	< .001
I have no appetite during the day.	.30	.06	4.87	< .001
I worry about sleeping.	.09	.06	1.52	.461
I didn't have enough sleep last night.	.10	.07	1.47	.483
I am restless.	.21	.06	3.33	.020
I am tired.	-.08	.06	-1.27	.584
It is not effortful to do things.	-.05	.08	-.58	.859
I feel guilty.	.13	.12	1.08	.672
I am doing things at my normal pace.	.35	.08	4.29	.001
I feel worthless.	.35	.06	5.63	< .001
I feel that I can't get anything done.	.22	.07	3.09	.035
I feel that I can't make decisions.	.27	.10	2.70	.097
I can't concentrate.	.20	.06	3.19	.027
I feel hopeless.	.32	.06	5.47	< .001
How's your day?	.18	.06	2.96	.047
How would you rate your overall physical health today?	.12	.08	1.41	.504

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 3.11 *Meta-analysis of standardized betas of age predicting DDI item variability in the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	-.26	.13	-2.00	.255
I feel sad.	-.10	.07	-1.49	.475
I feel irritable.	-.08	.07	-1.09	.670
I enjoy what I am doing.	-.22	.06	-3.46	.016
I don't care about anything.	-.15	.06	-2.26	.203
I have no appetite during the day.	-.17	.07	-2.40	.163
I worry about sleeping.	-.05	.07	-.78	.810
I didn't have enough sleep last night.	-.03	.07	-.45	.892
I am restless.	-.13	.07	-1.88	.293
I am tired.	.00	.07	.05	.990
It is not effortful to do things.	-.12	.08	-1.49	.475
I feel guilty.	-.26	.13	-2.00	.255
I am doing things at my normal pace.	-.16	.09	-1.71	.373
I feel worthless.	-.15	.07	-2.25	.203
I feel that I can't get anything done.	-.17	.08	-2.03	.255
I feel that I can't make decisions.	-.26	.11	-2.36	.177
I can't concentrate.	-.15	.07	-2.20	.225
I feel hopeless.	-.21	.06	-3.20	.027
How's your day?	-.14	.07	-2.02	.255
How would you rate your overall physical health today?	-.10	.10	-1.07	.676

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 3.12 *Meta-analysis of standardized betas of gender predicting DDI item variability in the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	-.27	.25	-1.08	.672
I feel sad.	-.27	.14	-2.00	.255
I feel irritable.	-.20	.14	-1.46	.483
I enjoy what I am doing.	-.24	.13	-1.81	.326
I don't care about anything.	-.14	.13	-1.03	.693
I have no appetite during the day.	-.08	.14	-.62	.829
I worry about sleeping.	-.06	.14	-.42	.897
I didn't have enough sleep last night.	-.15	.15	-1.00	.699
I am restless.	-.16	.14	-1.11	.660
I am tired.	-.24	.14	-1.74	.355
It is not effortful to do things.	-.27	.18	-1.53	.461
I feel guilty.	.04	.25	.16	.960
I am doing things at my normal pace.	.17	.18	.92	.728
I feel worthless.	-.02	.14	-.16	.960
I feel that I can't get anything done.	-.35	.16	-2.18	.227
I feel that I can't make decisions.	-.43	.21	-2.05	.255
I can't concentrate.	-.41	.13	-3.03	.041
I feel hopeless.	-.17	.13	-1.28	.580
How's your day?	-.13	.14	-.98	.701
How would you rate your overall physical health today?	-.39	.18	-2.14	.248

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 3.13 *Meta-analysis of standardized betas of educational attainment predicting DDI item variability in the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	-.03	.12	-.25	.943
I feel sad.	.08	.07	1.17	.640
I feel irritable.	-.01	.06	-.15	.960
I enjoy what I am doing.	-.02	.06	-.35	.913
I don't care about anything.	.02	.06	.25	.943
I have no appetite during the day.	.12	.06	1.89	.293
I worry about sleeping.	-.05	.06	-.82	.787
I didn't have enough sleep last night.	-.07	.07	-1.00	.699
I am restless.	.02	.06	.29	.943
I am tired.	-.12	.06	-1.93	.279
It is not effortful to do things.	.01	.08	.13	.964
I feel guilty.	.05	.12	.42	.897
I am doing things at my normal pace.	-.01	.09	-.16	.960
I feel worthless.	.08	.06	1.28	.581
I feel that I can't get anything done.	-.10	.08	-1.30	.578
I feel that I can't make decisions.	-.08	.10	-.80	.796
I can't concentrate.	-.06	.06	-.93	.728
I feel hopeless.	.10	.06	1.60	.417
How's your day?	.01	.06	.20	.957
How would you rate your overall physical health today?	-.13	.09	-1.42	.504

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 3.14 *Meta-analysis of standardized betas of marital status predicting DDI item variability in the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	.19	.26	.73	.816
I feel sad.	-.01	.13	-.06	.990
I feel irritable.	.03	.13	.24	.943
I enjoy what I am doing.	.12	.13	.93	.728
I don't care about anything.	-.17	.12	-1.39	.519
I have no appetite during the day.	-.04	.13	-.32	.939
I worry about sleeping.	-.11	.14	-.80	.796
I didn't have enough sleep last night.	-.01	.14	-.09	.980
I am restless.	.00	.13	-.02	.990
I am tired.	.02	.13	.17	.960
It is not effortful to do things.	-.13	.16	-.83	.787
I feel guilty.	.01	.26	.04	.990
I am doing things at my normal pace.	-.10	.19	-.51	.881
I feel worthless.	-.06	.13	-.48	.884
I feel that I can't get anything done.	-.16	.15	-1.10	.667
I feel that I can't make decisions.	-.32	.22	-1.45	.483
I can't concentrate.	-.18	.13	-1.35	.553
I feel hopeless.	-.11	.13	-.86	.764
How's your day?	.02	.13	.12	.966
How would you rate your overall physical health today?	-.20	.19	-1.04	.687

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 3.15 *Meta-analysis of standardized betas of employment status predicting DDI item variability in the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	.26	.36	.72	.816
I feel sad.	-.09	.15	-.60	.845
I feel irritable.	-.14	.15	-.93	.728
I enjoy what I am doing.	-.10	.14	-.67	.822
I don't care about anything.	-.11	.14	-.76	.812
I have no appetite during the day.	.04	.15	.30	.943
I worry about sleeping.	-.10	.15	-.67	.822
I didn't have enough sleep last night.	.14	.16	.86	.766
I am restless.	-.07	.15	-.44	.894
I am tired.	-.32	.15	-2.11	.252
It is not effortful to do things.	-.13	.18	-.77	.810
I feel guilty.	.70	.35	2.00	.255
I am doing things at my normal pace.	-.04	.22	-.19	.960
I feel worthless.	-.06	.15	-.43	.897
I feel that I can't get anything done.	-.20	.16	-1.20	.633
I feel that I can't make decisions.	.70	.30	2.33	.183
I can't concentrate.	-.08	.15	-.55	.873
I feel hopeless.	-.07	.15	-.49	.884
How's your day?	-.01	.15	-.07	.986
How would you rate your overall physical health today?	-.04	.23	-.18	.960

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Discussion

Consistently significant as well as consistently insignificant results were found in the three studies. MD severity as represented by PHQ-9 score consistently significantly predicted variability of several MD symptoms while the predictability of other moderators including age, gender, educational attainment, marital status, and employment status on MD symptom variability was mostly insignificant.

The hypothesis of high symptom variability reflected MD severity as measured by PHQ-9 score was thus marginally to partially supported across studies. However, the results revealed heterogeneity among MD symptoms because MD severity only significantly predicted the variability of some MD symptoms: 10 symptoms in Study 1, one in Study 2, one in Study 3, and 12 in the meta-analysis. This echoed the findings in van Eeden, van Hemert, Carlier, Penninx, and Giltay

(2019). They reported noticeable within-person MD symptom variability in a 9-year follow-up study of MD patients. Since PHQ-9 score is the sum-total of all MD symptoms, one possible explanation for the varying relationships between MD symptoms and MD severity might be that participants' ratings on the MD symptoms that were not significantly predicted by PHQ-9 score may contribute less to PHQ-9 score. Correlating standardized betas of PHQ-9 scores and other moderators extracted from regression models across the three studies showed only the results of PHQ-9 score were moderately to highly correlated, inferring reproducibility (Table 3.9; Figures 1–6 in Appendix C).

The inter-correlations of DDI item variabilities were explained by the first principal component by 54%, 45%, and 42% in the three studies. These somewhat variable but consistently comparatively high percentages implied certain level of homogeneity among the symptoms in their fluctuating behavior. Nonetheless, the PCA loadings of the DDI items spread a wide range may suggest that even though the first principal component explained a great amount of total variances, the amount of variance explained by it in each DDI item diverged enormously. Hence, the items were affected by the first principal component differently and MD symptoms were at least partly heterogeneous in their fluctuating behavior, consistent with some underlying heterogeneity in depression mechanisms. The correlations of the PCA loadings from the three studies revealed high inter-correlations of the variability in MD symptoms, showing homogeneity in the fluctuations of MD symptom variability (Table 3.9).

The seemingly contradictory results of homogeneity and heterogeneity of MD symptoms may be caused by the frequency and duration of data collection in the three studies, the participants being mostly healthy adults, and/or the chosen measure of variability. Some studies reported symptom variability adopted a longer and less frequent period of data collection, such as once a week for eight weeks (Dawood & Pincus, 2017), once a month for three years (Karp et al., 2004), five times within nine years (van Eeden et al., 2019), and once a year for 12 years (Melhem et al., 2019). In the three studies in this chapter, the frequency of data

collection was 4-6 times per day for two weeks, which is relatively frequent and short compared to the aforementioned studies. Some changes and events might take longer to manifest and longer period of data collection would be required to capture these changes (D. E. Stull et al., 2009). Though using participants not diagnosed with mental disorders might invoke the discrepancy, van Eeden et al. (2019) employed university student participants but obtained supporting results for the associations between pathological narcissism and higher MD symptom variability and instability. The different measures of symptom variability used in these studies included fraction of variance unexplained (van Eeden et al., 2019), coefficient of variation of sum scores (standard deviation/mean × 100) (Karp et al., 2004), intra-individual standard deviation (Dawood & Pincus, 2017), and *hlme* function in R (Melhem et al., 2019). In addition, different measures for MD used across studies may complicate the interpretation of the results in these studies. These disparities may explain the seemingly contradictory findings reported in this chapter but the finding may display the actual heterogeneous nature of MD symptoms –sometimes heterogeneous and sometimes homogeneous.

Some MD symptoms were found to be congruently less or more variable across the three studies as shown in the overall standard deviations (Table 3.1). Feeling sad had a low standard deviation. Feeling tired, worrying about sleeping, and feeling did not have enough sleep last night had relatively high standard deviations. High variability in sleep related symptoms was reported in Karp et al. (2004) and van Eeden et al. (2019). Different from the results in this chapter, suicidal ideation was the most stable among the MD symptom in these two studies. MD patients had suicidal ideation in the baseline survey continued to have suicidal ideation in follow-ups. The patients who did not have suicidal ideation initially also did not have suicidal ideation in the follow-ups. Karp et al. (2004) suggested high symptom variability might be a trait because no variability was found between different treatment groups. Karp et al. (2004)'s trait explanation may be extended to symptom level – each individual may innately express some symptoms (low variability) but one may develop other symptoms as the disorder progress (high

variability). This would provide further support the MD symptom heterogeneity hypothesis.

Significant results of linear models, replicability analysis and meta-analysis were mostly found between PHQ-9 score and MD symptom variabilities and the results of other moderators were predominately insignificant. These may be explained as homogeneity among MD symptoms. However, significant results were not found in all MD symptoms and even though the first principal components explained a great amount of the variances in PCA analyses, the wide range of PCA loadings may denote heterogeneity in MD symptoms. Overall, these results supported the view of MD symptoms are to some extent homogeneous, whereas there is also support for dis-uniformity among symptoms which may eventually conveying the heterogeneity of MD.

Limitations

The majority of the participants were university students, which limited the scope of the generalizability of the results for nearly all the moderators, especially age, marital status, employment status, and educational attainment. Most of the participants were in their early twenties so if they are diagnosed with MD, they must have the early-onset type of MD. However, the exact age of onset was not measured. Female dominance in the participants hindered the test on sex differences in MD. The participants were mainly comprised of single students, which made it hard to compare the influences of employment status, marital status, and educational attainment had on MD variability.

Among the moderators discussed in this chapter, age and gender were also significant predictors for variability of one item in the DDI in Study 3 and in Study 2, respectively. Other moderators were not significant predictors for any items in the DDI. The limitations stated above may be the cause.

In addition, the moderators measured in the studies could only reflect features that do not change over time. For instance, within-individual changes in socio-economic measures including financial strain, property, deprivation, and living arrangements showed greater changes in MD symptomatology as those measures

went downward more than symptom improvement when these conditions advance (Lorant et al., 2007). This is because longitudinal studies only revealed moderate within-individual variations in socio-economic measures comparing to between-individual changes in cross-sectional studies (Lorant et al., 2007). Including more detailed measurements of moderators that reflect changes of time may yield more robust results.

Future directions

Males are affected by behavioral disorders while females usually experience affective disorders. Several theories were proposed to explain the possible mechanism of the differences. However, a satisfying conclusion has yet to be met due to ample evidences from both sides (T. D. Hill & Needham, 2013). To tackle the problem of sex difference in MD, developing a separate set of diagnostic criteria may be needed to decrease the rate of underdiagnoses in males and enhance their wellbeing.

The next chapter will look into the relationships between momentary ratings of MD symptoms, different measuring times of MD symptoms (e.g., morning, afternoon, and evening), and MD severity.

Chapter 4 Relationships between MD and circadian rhythm

Introduction

Circadian rhythm

The nature operates according to 24-hour cycle daily and four seasons yearly. To adapt to this 24-hour rhythm, organisms ranging from single cell, plants, insects, animals, to humans also abide by the daily or seasonal cycles and have cyclic physiological changes, circadian rhythm. The controlling center of these cyclic changes is located in the suprachiasmatic nuclei (SCN) in the hypothalamus (Hastings, 1997; Moore & Eichler, 1972; Stephan & Zucker, 1972). These cyclic changes is regulated by oscillators located in both the brain and peripheral tissues (Dolatshad et al., 2006; King et al., 1997; Matsuo et al., 2003; Yamazaki et al., 2000). The SCN send neural signals and secret hormones such as cortisol and melatonin to modulate and sync cyclic physiological changes with the natural day-night cycle (Monteleone et al., 2011). This results in entrainment, synchrony between internal physiological changes with the external day-night cycle in the surrounding environments. In humans, the most palpable examples of circadian rhythm are sleep-wake cycle, body temperature, and feeding.

Besides the natural day/night length changes, circadian rhythm is also modulated by jet lag, daylight saving time (DST), and shift work. People experience these when they travel across continents, live in countries practicing DST, or work in night shifts – outside of usual working hours of 7 a.m. to 6 p.m. Traveling to a different time zone creates misalignment between human internal circadian clock and the outer environment. But the effect of jet lag is moderated by the number of time zones one travelled across, age, and whether the time difference is backward of forward comparing to the departure city (Baron & Reid, 2014). Lengthening a 24-hour day by one hour did not affect people's sleep when they experience DST in the autumn. But more people reported being influenced by the shortening of a 24-hour

day during the spring DST, especially in the first week after the clock was adjusted backward (Kantermann et al., 2007; Lahti et al., 2006).

What are influenced by circadian rhythm?

Circadian rhythm is also associated with subjective well-being (Boivin et al., 1997) and mood (Murray et al., 2002). Positive affect have been observed to fluctuate in accordance with circadian rhythm but this has not been reported in negative affect (Murray, 2007). The symptoms of many diseases or psychiatric disorders also exhibit a circadian rhythm (Smolensky et al., 2015).

Some diurnal variations in MD symptoms have been reported but controversies remain. For example, some studies observed significant morning mood worsening in MD patients (Murray, 2007; von Knorring et al., 1977) while others reported insignificant results (Gordijn et al., 1994; Tölle & Goetze, 1987). People do not have MD usually experience worsening mood in the evening. Also, Kammerer, Taylor, and Glover (2006) noticed distinct mood patterns in pregnant women diagnosed with either one of the two different subtypes of MD – those suffering from melancholic depression showed morning mood worsening and those having atypical depression exhibited evening mood worsening. Patients with these two different subtypes of MD also exhibited opposite symptoms, cortisol levels, and inflammatory and metabolic dysregulation (Kammerer et al., 2006; Lamers et al., 2013). Davidson and Turnbull (1986) also found morning mood worsening were among the mostly frequently reported symptoms in melancholic depression patients than in non-melancholic patients. But they reported opposite findings in the same paper, too. They explained the controversy results may be caused by MD symptoms had progressed in severity (Waldman, 1972). However, other studies have found no connections between diurnal mood variations and MD severity (Carpenter et al., 1986; Peeters et al., 2006). Therefore, whether mood variation, especially morning mood worsening is correlated with MD seemed to be under debate.

Besides mood, circadian variations have been observed in other MD symptoms such as core body temperature, cortisol level, melatonin level, sleep-wake cycle, and motor activity (Monteleone et al., 2011; Vadnie & McClung, 2017).

Desynchronization of circadian rhythm and health

Circadian disturbances or misalignment is associated with poor physical and mental health. It also has being associated with physical diseases and psychiatric disorders including MD (Baron & Reid, 2014; Wirz-Justice, 2006, 2008). Treatments used to adjust circadian rhythm such as low-dose ketamine and sleep deprivation therapy both showed rapid effect in reducing depressive symptoms including suicidal ideation in a MD subgroup, which exhibited desynchronized circadian rhythms (B G Bunney & Bunney, 2012; B G Bunney et al., 2015). In a review of 17 clinical trials, low-does ketamine intravenous injection swiftly decreased depressive symptoms in treatment-resistant MD and bipolar depressed patients (B G Bunney & Bunney, 2012). Ketamine might act as a glutamate N-methyl-D-Aspartate (NMDA) antagonist, which increases synaptic plasticity and resulting in a fast effect on depressive symptoms (Browne & Lucki, 2013; Gerhard et al., 2016; Kavalali & Monteggia, 2012). NMDA administration to the SCN has been shown to induce phase-shift in vitro (Shibata et al., 1994) and in vivo (Mintz et al., 1999). Neural cell culture studies also showed ketamine could regulate clock genes (Bellet et al., 2011). Misalignment of circadian rhythm may cause MD in some MD patients.

Research on circadian typology also showed a link between evening chronotype and MD. In the three circadian typologies of morning, intermediate, and evening chronotypes, people with an evening chronotype were more likely to suffer from MD (Kantermann et al., 2012). Also, the association between MD and evening chronotype remained significant after controlling for confounders such as social demographics, physical health, and sleep factors including insomnia and average duration of sleep. Circadian typology is determined by individual's bed time, wake time, and the times when people perform the best physically and mentally (Adan et al., 2012). People with morning chronotype like to start their days early, they reach their optimal physical or mental performance in the early part of a day, and they go

to bed early as well. Those having evening chronotype tend to get up late, reach their best physical and mental performance at the end of a day, and go to bed late. Others who do not fit into the morning or evening chronotypes have an intermediate chronotype. The results on the association between anxiety and chronotype is inconsistent. Some studies found the association (Antypa et al., 2016; Lemoine et al., 2013) while others did not (Kantermann et al., 2012). A meta-analysis analyzed the effect sizes of morningness or morningness-eveningness in 36 papers covered several psychiatric disorders including MD, bipolar disorder, seasonal affective disorder (SAD), and multiple mood disorders. The authors also controlled for publication bias to reassure the effects and their results showed MD severity was only associated with an evening chronotype but was not related to a morning or an intermediate chronotype (Au & Reece, 2017).

The discovery of the relationship between circadian rhythm and MD encouraged the development of new treatment approaches such as light therapy, new antidepressants, and wake therapy (Monteleone et al., 2011). The development of a new class of drugs targeting melatonin such as agomelatine was one of these new treatments (de Bodinat et al., 2010; Hickie & Rogers, 2011). Agomelatine has prominent antidepressant effects, possibly because it not only works on melatonin receptors to adjust circadian rhythm but also a serotonin antagonist, which prevents serotonin reabsorption by cells and helps to maintain a high concentration of serotonin in the space between cells. Increasing serotonin level has long been the target of MD medication and the frontline antidepressants were designed to tackle various types of serotonin receptors. Developing antidepressants targeting several mechanisms or symptoms may be a potentially fruitful approach in MD treatment (Millan, 2006).

Among the circadian theories explaining MD, most of the theories either lack or have limited supporting empirical evidences (Germain & Kupfer, 2008). Only one of the theories – the phase-shift hypotheses of depression – has reassuring results, especially in treating people suffering from summer SAD or winter depression (Lam & Levitan, 2000). SAD was firstly discovered in people with MD symptoms as well as

atypical MD symptoms during changing seasons particularly in winter but some people also had atypical MD symptoms in summer. However, SAD is different from atypical depression and MD (Westrin & Lam, 2007) so strictly speaking, none of the circadian theories of MD provided satisfactory explanations for MD.

The literature on the relationships between circadian rhythm and MD symptoms has been controversial and the relationship has yet been well established. This chapter focuses on disentangling the relationships between circadian rhythm and MD symptoms by looking closely at the relationship between circadian rhythm and each MD symptom separately. In three studies, the momentary MD symptom ratings are firstly grouped into – morning, afternoon, and evening – according to the time participants gave these ratings and then these ratings were compared with each other within individual participants. We hypothesize MD symptoms would have varied patterns of circadian rhythm in terms of mean-level differences across the times of day (which would be consistent with MD not being an ontologically coherent entity) and these different diurnal patterns in MD symptoms should correspond with MD severity (e.g., morning mood worsening) (H11). Heterogeneity in MD symptom would find support if varied patterns were observed in the relationships between circadian rhythm and individual MD symptoms.

Materials and Method

The participants, materials, and procedure in the three studies were the same as those described in Studies 1, 2, and 3 in Materials and Method in Chapters 2 and 3.

Results

To analyze the relationship between MD severity and circadian rhythm as shown in momentary ratings of MD symptoms taken in mornings, afternoons, and evenings, three linear mixed-effect models were employed. The analyses were carried out using lme4 package (Version 1.1-17) in RStudio. The use of linear mixed-effect models allowed controlling for variations in repeated measures within each

participant (Baayen, Davidson, & Bates, 2008; Magezi, 2015). Rather than building the models hierarchically, the same three models were used to test each DDI items and the best-fit models among the three as well as the best-fit model for most of the DDI items were reported. The latter was used as a common model to compare the standardized betas between the DDI items.

Since MD severity measured by using PHQ-9 score was the most significant predictor of MD symptom variability as reported in Chapter 3, PHQ-9 score was included in the three linear mixed-effect models as a moderator of the momentary MD symptom ratings. In one of the models, the relationship between circadian rhythm and MD severity were tested using the interactions between PHQ-9 score and the measuring times.

Model 1 was the simplest model and it included fixed factors of PHQ-9 score, age, gender, educational attainment, marital status, employment status, and the time of answering the questionnaire, and a random intercept factor for participants. Model 2 consisted of fixed factors including PHQ-9 score, age, gender, educational attainment, marital status, employment status, and the time of answering the questionnaire and a random factor of the effect of time within each participant. In Model 3, fixed factors were age, gender, educational attainment, marital status, employment status, the time of response, PHQ-9 score, and the interaction between PHQ-9 score and the time of answering the questionnaire. Participant was the random intercept factor in this model. In the three models, the DVs were the momentary ratings of the Daily Depression Items (DDI). The DDI items that only recorded once a day including "*I have no appetite during the day*", "*I worry about sleeping*", "*I feel that I didn't have enough sleep last night*", "*How's your day*", and "*How would you rate your overall physical health today*" were excluded from the analyses. PHQ-9 score was included in the models because it was a significant predictor of variability in many items in the DDI as tested in Chapter 3 because PHQ-9 might be a significant predictor of the momentary ratings of the DDI items, too. The level of measurement for the IVs was the same as those in Chapter 3, where educational attainment was continuous, marital status only had two levels of single,

divorced, and widowed in one level and in a relationship and married in another, and employment status had two levels of employed or self-employed, and full-time student and part-time employed, retired, and unemployed. All continuous variables including the DDI items, PHQ-9 score, age, and educational attainment were grand-mean centered in the three models. The Akaike information criterion (AIC) was used to select the best model that predicted the momentary ratings of the DDI items, where the lowest AIC indicated a superior model. However, there were no variances between random effects in five items in the three studies so even though Model 2 was the best-fit model according to the AIC, Model 1 was indeed the best-fit model for these items. These items were "*I feel sad*", "*It is not effortful to do things*", and "*I feel that I can't get anything done*" in Study 1, "*I am tired*" in Study 2, and "*I feel irritable*" in Study 3. All *p*-values reported in this chapter were adjusted using false discovery rate (FDR) to correct for multiple comparison. The R codes of the models were listed in Appendix B.

Study 1

Model 1 was the best-fit for five DDI items and Model 2 was the best-fit for the other six DDI items. Model 2 did not converge when testing the relationships between the predictors and the momentary ratings of "*I can't concentrate*" and this model was discarded. The best-fit model for this item was decided by comparing the AICs of Models 1 and 3. The coefficients for PHQ-9 scores in the linear mixed-effect models were significant for all the DDI items. PHQ-9 score was a significant predictor for the momentary ratings of MD symptoms. Table 4.1 lists the best-fit model, standardized beta, intraclass correlation coefficient, and *p*-value for each DDI item.

Only five items had significant standardized betas for the afternoon (Table 4.2) and evening measuring times (Table 4.3) from the best-fit linear mixed-effect models. These items were four shared items – "*I feel sad*", "*I feel irritable*", "*I enjoy what I am doing*", and "*I don't care about anything*" – and "*I feel restless*" for the

afternoon measuring time and "*I am tired*" for the evening measuring time. Measuring time did not have huge influence over MD symptoms.

To take a closer look at the diurnal changes in the six DDI items with significant standardized betas for the afternoon and evening measuring times, the means and standard deviations were compared (Table 4.4). Worsening mood in the morning as reported in some research was observed in this study. Participants felt sadder and were more irritable in the mornings than they did in the afternoons and evenings. The evening mood fluctuated the most between the three measuring times. In the mornings, participants had low interest or pleasure as seen in the means of enjoying the things one was doing and caring about things. These may be affected by poor morning mood. Enjoying what one was doing changed the most in the afternoons while caring about things fluctuated more in the evenings. Feeling restless was rated the highest in the evenings but it changed the most in the mornings. On average, people felt the most tired in the afternoons and feeling tired varied the greatest in the evenings. Different types of evening activities or different amount of energy being consumed during daytime may be possible causes. MD symptom heterogeneity could be observed in diurnal changes, too. These different diurnal patterns did not correspond with MD severity as measured using PHQ-9 score, which is the sum of all MD symptoms. This supported MD symptom heterogeneity.

Either Models 1 or 2 emerged to be the best-fit model of the DDI items might imply the items are heterogeneous. However, having the standardized betas of the DDI items from different models means we cannot compare them. Since Model 1 was the best-fit model for the majority of the DDI items, to compare the items, the standardized betas were extracted from Model 1 (Table 4.5 – 4.7).

In summary, for all the DDI items, grand-mean centered PHQ-9 score significantly predicted the momentary ratings. Diurnal variations were inconsistently observed in a few items in the afternoon and evening measuring times as compared to the morning measuring time. Since Model 3, the multilevel model testing the interactions between MD severity and measuring times, was not

the best-fit for all DDI items, the part of H11 regarding the coincidences between diurnal patterns in MD symptoms and MD severity cannot be verified. The mean and standard deviations of momentary ratings of these items did show variances between measuring times. Heterogeneity in MD symptoms were observed in some DDI items that were significantly affected by the afternoon and the evening measuring times, and the means and standard deviations of some DDI items.

Two more studies were conducted to test the results of Study 1.

Table 4.1 *Standardized betas and p-values of PHQ-9 score from the best-fit linear mixed-effect models in Studies 1, 2, and 3*

Study	Study 1				Study 2				Study 3			
DDI item	Model	*β*	*ICC*	*p*	Model	*β*	*ICC*	*p*	Model	*β*	*ICC*	*p*
I feel happy.	-	-	-	-	-	-	-	-	1	.48	.30	< .001
I feel sad.	1	.43	.32	< .001	1	.20	.34	.019	1	.53	.34	< .001
I feel irritable.	2	.40	.32	< .001	1	.14	.30	.072	1	.30	.39	.002
I enjoy what I am doing.	2	.39	.27	< .001	1	.13	.27	.089	2	.44	.24	< .001
I don't care about anything.	1	.23	.42	< .001	1	.24	.38	.004	1	.48	.57	< .001
I have no appetite during the day.	-	-	-	-	-	-	-	-	-	-	-	-
I worry about sleeping.	-	-	-	-	-	-	-	-	-	-	-	-
I feel that I don't have enough sleep last night.	-	-	-	-	-	-	-	-	-	-	-	-
I am restless.	1	.35	.37	< .001	1	.22	.36	.013	2	.23	.36	.002
I am tired.	2	.37	.31	< .001	1	.17	.30	.028	2	.21	.30	.002
It is not effortful to do things.	1	.25	.43	< .001	1	.15	.40	.110	-	-	-	-
I feel guilty.	-	-	-	-	-	-	-	-	1	.48	.44	< .001
I am doing things with my normal pace.	-	-	-	-	1	.24	.29	.002	2	.24	.39	.004
I feel worthless.	1	.54	.38	< .001	1	.34	.45	< .001	1	.65	.48	< .001
I feel that I can't get anything done.	1	.40	.35	< .001	1	.24	.27	< .001	-	-	-	-
I feel that I can’t make decisions.	-	-	-	-	-	-	-	-	1	.60	.45	< .001
I can't concentrate.	1	.42	.36	< .001	1	.28	.29	< .001	2	.54	.36	< .001
I feel hopeless.	1	.53	.38	< .001	1	.35	.40	< .001	1	.72	.42	< .001
How's your day?	-	-	-	-	-	-	-	-	-	-	-	-
How would you rate your overall physical health today?	-	-	-	-	-	-	-	-	-	-	-	-

Note. Model = the best-fit model for each DDI item; *β* = standardized beta of the fixed effect; *ICC* = adjusted intraclass correlation coefficient; *p* = *p*-value.

Table 4.2 *Standardized betas and p-values of afternoon measuring time from the best-fit linear mixed-effect models in Studies 1, 2, and 3*

Study	Study 1			Study 2			Study 3		
DDI item	Model	*β*	*p*	Model	*β*	*p*	Model	*β*	*p*
I feel happy.	-	-	-	-	-	-	1	-.05	.156
I feel sad.	1	-.08	< .001	1	.03	.611	1	-.02	.688
I feel irritable.	2	-.11	.002	1	.01	.777	1	.00	.956
I enjoy what I am doing.	2	-.09	.011	1	-.07	.145	2	-.02	.637
I don't care about anything.	1	-.08	< .001	1	.05	.183	1	-.03	.307
I have no appetite during the day.	-	-	-	-	-	-	-	-	-
I worry about sleeping.	-	-	-	-	-	-	-	-	-
I feel that I don't have enough sleep last night.	-	-	-	-	-	-	-	-	-
I am restless.	1	.10	< .001	1	.03	.509	2	.05	.175
I am tired.	2	-.06	.279	1	-.04	.453	2	.08	.048
It is not effortful to do things.	1	-.01	.803	1	.03	.457	-	-	-
I feel guilty.	-	-	-	-	-	-	1	.04	.217
I am doing things with my normal pace.	-	-	-	1	.05	.252	2	.01	.755
I feel worthless.	1	-.01	.684	1	.07	.030	1	-.01	.706
I feel that I can't get anything done.	1	-.05	.065	1	.01	.853	-	-	-
I feel that I can’t make decisions.	-	-	-	-	-	-	1	.00	.912
I can't concentrate.	1	-.02	.499	1	.06	.183	2	.05	.183
I feel hopeless.	1	-.01	.755	1	.03	.556	1	.01	.658
How's your day?	-	-	-	-	-	-	-	-	-
How would you rate your overall physical health today?	-	-	-	-	-	-	-	-	-

Note. Model = the best-fit model for each DDI item; *β* = standardized beta of the fixed effect; *p* = *p*-value.

Table 4.3 *Standardized betas and p-values of evening measuring time from the best-fit linear mixed-effect models in Studies 1, 2, and 3*

Study	Study 1			Study 2			Study 3		
DDI item	Model	*β*	*p*	Model	*β*	*p*	Model	*β*	*p*
I feel happy.	-	-	-	-	-	-	1	-.15	< .001
I feel sad.	1	-.12	< .001	1	.03	.597	1	-.03	.457
I feel irritable.	2	-.14	< .001	1	.02	.748	1	-.10	.017
I enjoy what I am doing.	2	-.16	< .001	1	-.08	.084	2	-.15	.002
I don't care about anything.	1	-.07	.025	1	.10	.009	1	.02	.640
I have no appetite during the day.	-	-	-	-	-	-	-	-	-
I worry about sleeping.	-	-	-	-	-	-	-	-	-
I feel that I don't have enough sleep last night.	-	-	-	-	-	-	-	-	-
I am restless.	1	.04	.175	1	.02	.640	2	-.04	.488
I am tired.	2	.24	< .001	1	.13	.002	2	.41	< .001
It is not effortful to do things.	1	-.02	.470	1	-.01	.777	-	-	-
I feel guilty.	-	-	-	-	-	-	1	.01	.803
I am doing things with my normal pace.	-	-	-	1	.02	.681	2	.02	.755
I feel worthless.	1	-.01	.684	1	.04	.272	1	-.04	.183
I feel that I can't get anything done.	1	.02	.554	1	.05	.242	-	-	-
I feel that I can’t make decisions.	-	-	-	-	-	-	1	.00	.970
I can't concentrate.	1	.02	.642	1	.07	.100	2	.05	.457
I feel hopeless.	1	-.01	.777	1	.04	.304	1	-.01	.755
How's your day?	-	-	-	-	-	-	-	-	-
How would you rate your overall physical health today?	-	-	-	-	-	-	-	-	-

Note. Model = the best-fit model for each DDI item; *β* = standardized beta of the fixed effect; *p* = *p*-value.

Table 4.4 *Means and SDs of morning, afternoon, and evening measuring times for the six DDI items with a significant standardized beta of the afternoon and/or evening measuring time in linear mixed-effect models in Study 1*

DDI item	*Mean*			*SD*		
	M	A	E	M	A	E
I feel sad.	35.23	32.67	32.05	21.60	21.79	22.62
I feel irritable.	39.50	36.13	35.63	23.35	23.51	23.74
I enjoy what I am doing.	36.78	34.13	32.67	22.65	23.19	23.01
I don't care about anything.	30.44	28.21	28.56	22.26	21.52	22.51
I am restless.	51.56	49.28	58.14	29.36	28.99	28.45
I am tired.	38.06	40.36	39.07	25.28	26.90	26.98

Note. M = Morning; A = Afternoon; E = Evening.

Table 4.5 *Standardized betas and p-values of PHQ-9 score from Model 1 in Studies 1, 2, and 3*

Study	Study 1		Study 2		Study 3	
DDI item	*β*	*p*	*β*	*p*	*β*	*p*
I feel happy.	-	-	-	-	.48	< .001
I feel sad.	.43	< .001	.20	.019	.53	< .001
I feel irritable.	.40	< .001	.14	.072	.27	.002
I enjoy what I am doing.	.40	< .001	.13	.089	.41	< .001
I don't care about anything.	.23	< .001	.24	.004	.48	< .001
I have no appetite during the day.	-	-	-	-	-	-
I worry about sleeping.	-	-	-	-	-	-
I feel that I don't have enough sleep last night.	-	-	-	-	-	-
I am restless.	.35	< .001	.22	.013	.22	.007
I am tired.	.34	< .001	.17	.028	.20	.004
It is not effortful to do things.	.25	< .001	.15	.110	-	-
I feel guilty.	-	-	-	-	.48	< .001
I am doing things with my normal pace.	-	-	.24	.002	.25	.004
I feel worthless.	.54	< .001	.34	< .001	.65	< .001
I feel that I can't get anything done.	.40	< .001	.24	< .001	-	-
I feel that I can’t make decisions.	-	-	-	-	.60	< .001
I can't concentrate.	.42	< .001	.28	< .001	.52	< .001
I feel hopeless.	.53	< .001	.35	< .001	.72	< .001
How's your day?	-	-	-	-	-	-
How would you rate your overall physical health today?	-	-	-	-	-	-

Note. *β* = standardized beta of the fixed effect; *p* = *p*-value.

Table 4.6 *Standardized betas and p-values of afternoon measuring time from Model 1 in Studies 1, 2, and 3*

Study	Study 1		Study 2		Study 3	
DDI item	*β*	*p*	*β*	*p*	*β*	*p*
I feel happy.	-	-	-	-	-.05	.156
I feel sad.	-.08	< .001	.03	.611	-.02	.688
I feel irritable.	-.11	< .001	.01	.777	.00	.956
I enjoy what I am doing.	-.08	.002	-.07	.145	-.02	.637
I don't care about anything.	-.08	< .001	.05	.183	-.03	.307
I have no appetite during the day.	-	-	-	-	-	-
I worry about sleeping.	-	-	-	-	-	-
I feel that I don't have enough sleep last night.	-	-	-	-	-	-
I am restless.	.10	< .001	.03	.509	.05	.175
I am tired.	-.06	.048	-.04	.453	.08	.048
It is not effortful to do things.	-.01	.810	.03	.457	-	-
I feel guilty.	-	-	-	-	.04	.217
I am doing things with my normal pace.	-	-	.05	.252	.01	.755
I feel worthless.	-.01	.687	.07	.030	-.01	.706
I feel that I can't get anything done.	-.05	.067	.01	.853	-	-
I feel that I can’t make decisions.	-	-	-	-	.00	.912
I can't concentrate.	-.02	.499	.06	.183	.05	.183
I feel hopeless.	-.01	.761	.03	.556	.01	.658
How's your day?	-	-	-	-	-	-
How would you rate your overall physical health today?	-	-	-	-	-	-

Note. *β* = standardized beta of the fixed effect; *p* = *p*-value.

Table 4.7 *Standardized betas and p-values of evening measuring time from Model 1 in Studies 1, 2, and 3*

Study	Study 1		Study 2		Study 3	
DDI item	*β*	*p*	*β*	*p*	*β*	*p*
I feel happy.	-	-	-	-	-.15	< .001
I feel sad.	-.12	< .001	.03	.597	-.03	.457
I feel irritable.	-.15	< .001	.02	.748	-.10	.017
I enjoy what I am doing.	-.16	< .001	-.08	.084	-.16	< .001
I don't care about anything.	-.07	.025	.10	.009	.02	.640
I have no appetite during the day.	-	-	-	-	-	-
I worry about sleeping.	-	-	-	-	-	-
I feel that I don't have enough sleep last night.	-	-	-	-	-	-
I am restless.	.04	.175	.02	.640	-.05	.307
I am tired.	.24	< .001	.13	.002	.44	< .001
It is not effortful to do things.	-.02	.470	-.01	.777	-	-
I feel guilty.	-	-	-	-	.01	.803
I am doing things with my normal pace.	-	-	.02	.681	.02	.679
I feel worthless.	-.01	.684	.04	.272	-.04	.183
I feel that I can't get anything done.	.02	.554	.05	.242	-	-
I feel that I can’t make decisions.	-	-	-	-	.00	.970
I can't concentrate.	.02	.642	.07	.100	.05	.207
I feel hopeless.	-.01	.777	.04	.304	-.01	.755
How's your day?	-	-	-	-	-	-
How would you rate your overall physical health today?	-	-	-	-	-	-

Note. *β* = standardized beta of the fixed effect; *p* = *p*-value.

Study 2

As a replicate of Study 1, whether MD severity affects MD symptoms measured at different times was also tested here using linear mixed-effect models. The same three models used in Study 1 were used. Model 2 did not converge in three items – "*I am restless*", "*It is not effortful to do things*", and "*I feel worthless*" and these three models were removed. For these three items, model comparisons were conducted by comparing the AICs of Models 1 and 3.

Except three items "*I feel irritable*", "*I enjoy what I am doing*", and "*It is not effortful to do things*", the standardized betas of PHQ-9 score in linear mixed-effect models of all DDI items were significant (Table 4.1). Only one significant result was found in the standardized betas of the afternoon (Table 4.2) and the evening measuring times (Table 4.3). The item with significant result was "*I feel worthless*" in the afternoon measuring time and "*I don't care about anything*" in the evening measuring time. MD symptoms did showed varied diurnal patterns in momentary ratings but it was only slightly influenced by diurnal rhythm. The same as in Study 1, Model 3 containing an interaction term of measuring time and MD severity was not the best-fit for any DDI items so the relationship between different diurnal MD symptom patterns and MD severity was not tested.

One more study was used to verify the results of Studies 1 and 2.

Study 3

To further test the results of Studies 1 and 2, the same three multilevel models used in Studies 1 and 2 were employed. Model 2 of two DDI items "*I feel sad*" and "*I feel that I can't make decisions*" did not converge and they were removed. The AICs of Models 1 and 3 were used to select the best model of the two items.

Model 1 was the best-fit for seven DDI items while Model 2 was the best-fit for the other six items. PHQ-9 score was a significant predictor of the momentary ratings of DDI items in the linear mixed-effect models. The afternoon measuring time did not significantly predict any of the momentary ratings. The evening measuring time was a significant predictor of the momentary ratings for three DDI items "*I feel happy*", "*I enjoy what I am doing*", and "*I am tired*". There were diverse

diurnal patterns as well as a considerable amount of MD symptom heterogeneity. Nevertheless, due to Model 3 not being the best-fit for any of the DDI items, the correspondence between diurnal patterns in MD symptoms and MD severity cannot be examined.

Replicability across Studies 1, 2 and 3

Replicability of the results in Studies 1, 2, and 3 were tested using the Spearman's rank-order correlation and the standardized betas of PHQ-9 scores, the afternoon and the evening measuring times obtained from Model 1 of the three linear mixed-effect models. Table 4.5 shows the standardized betas of PHQ-9 score and the afternoon and the evening measuring times. The Spearman's rhos were shown in Table 4.6.

Between the three studies, the Spearman's rhos of the PHQ-9 score and the evening measuring time were median and high. The correlations between Studies 1 and 2 and between Studies 1 and 3 were above .50. Collectively, of course, these correlations were suggestive of a substantial degree of replication across the three independent groups of participants as it was very unlikely that three correlations of .50 and .60 and above would appear by chance even in a small sample of observations (here, standardized betas).

Table 4.8 *Standardized betas of PHQ-9 score and the afternoon and evening measuring times from Model 1 of the linear mixed-effect models in Studies 1, 2, and 3*

Study	Study 1			Study 2			Study 3		
DDI item	PHQ	Aft	Eve	PHQ	Aft	Eve	PHQ	Aft	Eve
I feel happy.	-	-	-	-	-	-	.48	-.05	-.15
I feel sad.	.43	-.08	-.12	.20	.03	.03	.53	-.02	-.03
I feel irritable.	.40	-.11	-.15	.14	.01	.02	.27	.00	-.10
I enjoy what I am doing.	.40	-.08	-.16	.13	-.07	-.08	.41	-.02	-.16
I don't care about anything.	.23	-.08	-.07	.24	.05	.10	.48	-.03	.02
I have no appetite during the day.	-	-	-	-	-	-	-	-	-
I worry about sleeping.	-	-	-	-	-	-	-	-	-
I feel that I don't have enough sleep last night.	-	-	-	-	-	-	-	-	-
I am restless.	.35	.10	.04	.22	.03	.02	.22	.05	-.05
I am tired.	.34	-.06	.24	.17	-.04	.13	.20	.08	.44
It is not effortful to do things.	.25	-.01	-.02	.15	.03	-.01	-	-	-
I feel guilty.	-	-	-	-	-	-	.48	.04	.01
I am doing things with my normal pace.	-	-	-	.24	.05	.02	.25	.01	.02
I feel worthless.	.54	-.01	-.01	.34	.07	.04	.65	-.01	-.04
I feel that I can't get anything done.	.40	-.05	.02	.24	.01	.05	-	-	-
I feel that I can’t make decisions.	-	-	-	-	-	-	.60	.00	.00
I can't concentrate.	.42	-.02	.02	.28	.06	.07	.52	.05	.05
I feel hopeless.	.53	-.01	-.01	.35	.03	.04	.72	.01	-.01
How's your day?	-	-	-	-	-	-	-	-	-
How would you rate your overall physical health today?	-	-	-	-	-	-	-	-	-

Note. PHQ = PHQ-9; Aft = Afternoon measuring time; Eve = Evening measuring time.

Table 4.9 *Spearman's rhos the standardized betas for PHQ-9 score and the afternoon and evening measuring times from Model 1 in Studies 1, 2, and 3*

Variables	*r*		
	Study1 vs. Study 2	Study 1 vs. Study3	Study2 vs. Study 3
PHQ-9 score	.56	.82	.64
Afternoon	.50	.53	-.05
Evening	.60	.67	.77

Note. *r* = Spearman's rho; *p* = p-value.

Meta-analysis

Meta-analysis was used to obtain robust results by examining the three studies collectively. Excluding the four DDI items only measured once a day, PHQ-9 score significantly associated with the momentary ratings of other 15 DDI items. The significance levels were smaller than .001 after adjusting for multiple comparison using FDR. The effect sizes of PHQ-9 score spanned from .22 ("*It is not effortful to do things*") to .60 ("*I feel that I can't make decisions*"), showing an extensive level of heterogeneity in the momentary ratings of MD symptoms (Table 4.7).

The afternoon and evening measuring times were significantly related to the momentary ratings of five DDI items (afternoon measuring time: Table 4.8; evening measuring time: Table 4.9). Some of these items were the same but some were different. The overlapping items were "*I feel sad",* "*I feel irritable*", and "*I enjoy what I am doing*". The different items were "*I don't care about anything*" and "*I am restless*" for the afternoon measuring time and "*I feel happy*" and "*I am tired*" for the evening measuring time. The effect sizes for measuring times were a mixture of positive and negative values. This may imply heterogeneity in MD symptoms, too. However, the differences between the effect sizes in the afternoon measuring time were relatively small of .13 (-.06–.07) compared to these in PHQ-9 score (.38) and the evening measuring time (.41). Therefore, MD symptom heterogeneity was less observable in the afternoon measuring time.

Table 4.10 *Meta-analysis of the standardized betas of PHQ-9 score from Model 1 in the three studies (N = 277)*

DDI item	*β*	*SE*	*Z*	*p*
I feel happy.	.48	.06	7.63	< .001
I feel sad.	.41	.03	11.87	< .001
I feel irritable.	.30	.04	8.60	< .001
I enjoy what I am doing.	.34	.03	11.03	< .001
I don't care about anything.	.29	.04	7.31	< .001
I have no appetite during the day.	-	-	-	< .001
I worry about sleeping.	-	-	-	< .001
I didn't have enough sleep last night.	-	-	-	< .001
I am restless.	.28	.04	7.42	< .001
I am tired.	.27	.03	8.41	< .001
It is not effortful to do things.	.22	.05	4.63	< .001
I feel guilty.	.48	.07	6.57	< .001
I am doing things at my normal pace.	.24	.05	4.73	< .001
I feel worthless.	.53	.04	15.03	< .001
I feel that I can't get anything done.	.34	.04	8.54	< .001
I feel that I can't make decisions.	.60	.07	8.57	< .001
I can't concentrate.	.41	.03	12.01	< .001
I feel hopeless.	.55	.03	16.27	< .001
How's your day?	-	-	-	-
How would you rate your overall physical health today?	-	-	-	-

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p* value.

Table 4.11 *Meta-analysis of the standardized betas of the afternoon measuring time from Model 1 in the three studies* (*N* = 277)

DDI item	*β*	*SE*	*Z*	*p*
I feel happy.	-.05	.03	-1.69	.156
I feel sad.	-.04	.02	-2.49	.026
I feel irritable.	-.05	.02	-3.21	.002
I enjoy what I am doing.	-.06	.02	-3.57	< .001
I don't care about anything.	-.03	.01	-2.33	.039
I have no appetite during the day.	-	-	-	-
I worry about sleeping.	-	-	-	-
I didn't have enough sleep last night.	-	-	-	-
I am restless.	.07	.02	4.17	< .001
I am tired.	-.02	.02	-.94	.470
It is not effortful to do things.	.00	.02	.27	.828
I feel guilty.	.04	.03	1.47	.217
I am doing things at my normal pace.	.03	.02	1.21	.324
I feel worthless.	.01	.01	.46	.739
I feel that I can't get anything done.	-.03	.02	-1.67	.160
I feel that I can't make decisions.	.00	.03	-.14	.912
I can't concentrate.	.01	.02	.90	.488
I feel hopeless.	.01	.01	.41	.755
How's your day?	-	-	-	-
How would you rate your overall physical health today?	-	-	-	-

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p* value.

Table 4.12 *Meta-analysis of the standardized betas of the evening measuring time from Model 1 in the three studies* (*N* = 277)

DDI item	*β*	*SE*	*Z*	*p*
I feel happy.	-.15	.04	-4.04	< .001
I feel sad.	-.06	.02	-3.25	.002
I feel irritable.	-.09	.02	-4.79	< .001
I enjoy what I am doing.	-.14	.02	-6.89	< .001
I don't care about anything.	.00	.02	.22	.853
I have no appetite during the day.	-	-	-	-
I worry about sleeping.	-	-	-	-
I didn't have enough sleep last night.	-	-	-	-
I am restless.	.02	.02	.82	.536
I am tired.	.26	.02	13.21	< .001
It is not effortful to do things.	-.02	.02	-.97	.457
I feel guilty.	.01	.03	.30	.803
I am doing things at my normal pace.	.02	.03	.79	.552
I feel worthless.	-.01	.02	-.63	.642
I feel that I can't get anything done.	.03	.02	1.45	.226
I feel that I can't make decisions.	.00	.03	.04	.970
I can't concentrate.	.04	.02	2.15	.058
I feel hopeless.	.00	.02	.12	.924
How's your day?	-	-	-	-
How would you rate your overall physical health today?	-	-	-	-

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p* value.

Discussion

Across the three studies and meta-analysis, MD severity measured using PHQ-9 score was a significant predictor of the momentary ratings of most MD symptoms. Three DDI items in Study 2 were the only exceptions. The predicting power of the afternoon and evening measuring times were not as prominent. For the afternoon measuring time, only five DDI items in Study 1, one in Study 2, five in meta-analysis yielded significant results. There were five DDI items in Study 1, one in Study 2, three in Study 3, and five in meta-analysis significantly predicted by the evening measuring time. This showed divergent predictability of measuring time in MD symptoms, suggesting heterogeneity in MD symptoms. Fluctuating diurnal patterns were found in the momentary ratings of some MD symptoms but the relationship between MD severity and diurnal patterns in MD symptoms was not

tested because the multilevel model that tested the interaction between MD severity and measuring time did not emerge to be the best model for any of the DDI items in the three studies.

The results of the three studies were highly reproducible as seen in PHQ-9 score and the evening measuring time. Replicability test using standardized betas and Spearman's rhos returned medium to high correlations for both PHQ-9 score and the evening measuring time in the three pairs of comparisons. Figures 4.1–4.3 show the standardized betas of PHQ-9, the afternoon measuring time, and the evening measuring time extracted from Model 1 in the three studies and meta-analysis, respectively. Similar patterns could be observed in some parts of the figures – between "*I can't concentrate*" and "*I feel hopeless*" in PHQ-9 score, between "*I am restless*", "*I am tired*", and "*It is not effortful to do things*" in the afternoon measuring time. The three comparable patterns in the evening measuring time were between "*I feel sad*", "*I feel irritable*", "*I enjoy what I am doing*", and "*I don't care about anything*", between "*I am restless*" and "*I am tired*", and between "*I can't concentrate*" and "*I feel hopeless*". Not all MD symptoms exhibited alike patterns might indicate MD symptom heterogeneity.

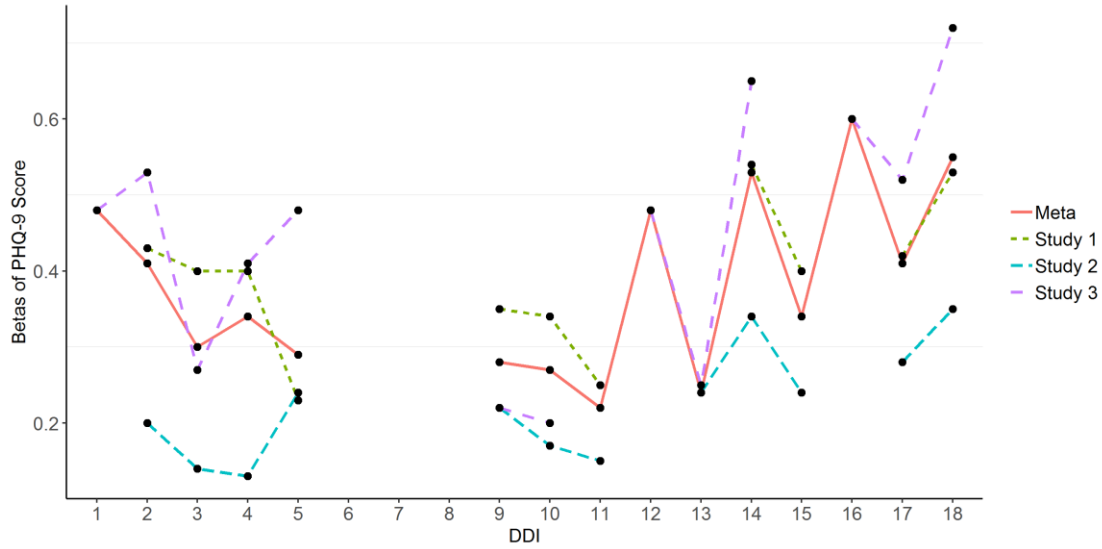


Figure 4.1 Standardized betas of PHQ-9 score from Model 1 in Studies 1, 2 and 3

Note. Each number on the x axis represents an item in the DDI. 1 = “I feel happy”; 2 = “I feel sad”; 3 = “I feel irritable”; 4 = “I enjoy what I am doing”; 5 = "I don't care about anything"; 6 = “I have no appetite during the day”; 7 = “I worry about sleeping”; 8 = “I didn’t have enough sleep last night”; 9 = "I am restless"; 10 = "I am tired"; 11 = "It is not effortful to do things"; 12 = “I feel guilty”; 13 = “I am doing things at my normal pace”; 14 = "I feel worthless"; 15 = "I feel that I can't get anything done"; 16 = “I feel that I can’t make decisions”; 17 = "I can't concentrate"; 18 = "I feel hopeless".

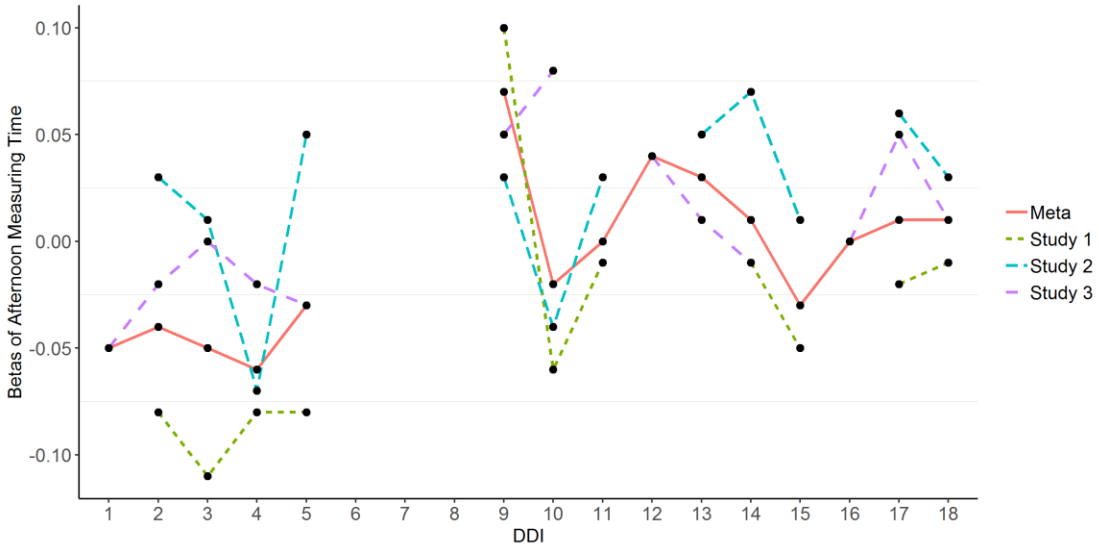


Figure 4.2 Standardized betas of the afternoon measuring time from Model 1 in Studies 1, 2 and 3

Note. Each number on the x axis represents an item in the DDI. 1 = “I feel happy”; 2 = “I feel sad”; 3 = “I feel irritable”; 4 = “I enjoy what I am doing”; 5 = "I don't care about anything"; 6 = “I have no appetite during the day”; 7 = “I worry about sleeping”; 8 = “I didn’t have enough sleep last night”; 9 = "I am restless"; 10 = "I am tired"; 11 = "It is not effortful to do things"; 12 = “I feel guilty”; 13 = “I am doing things at my normal pace”; 14 = "I feel worthless"; 15 = "I feel that I can't get anything done"; 16 = “I feel that I can’t make decisions”; 17 = "I can't concentrate"; 18 = "I feel hopeless".

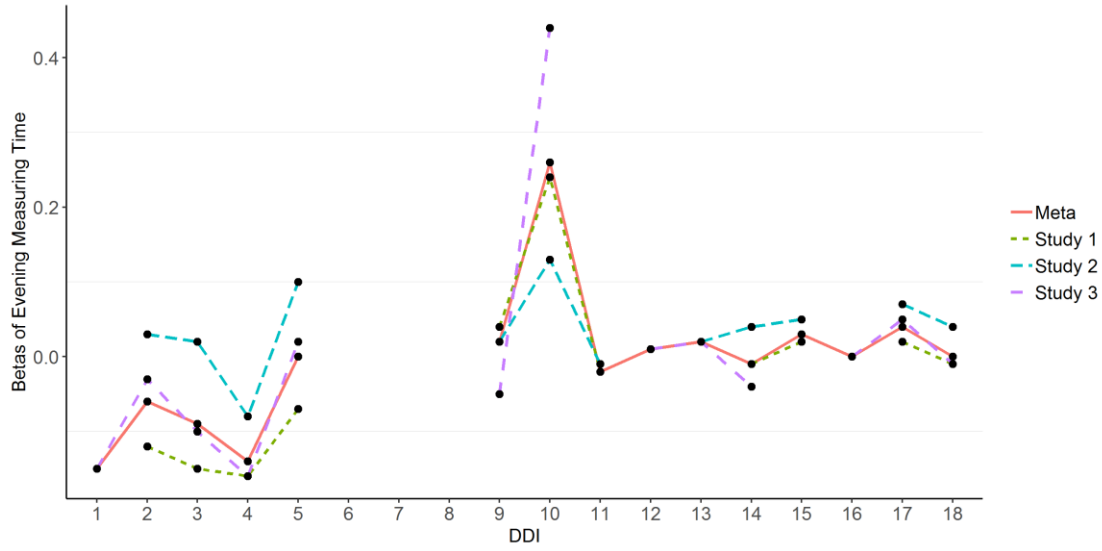


Figure 4.3 Standardized betas of the evening measuring time from Model 1 in Studies 1, 2 and 3

Note. Each number on the x axis represents an item in the DDI. 1 = “I feel happy”; 2 = “I feel sad”; 3 = “I feel irritable”; 4 = “I enjoy what I am doing”; 5 = "I don't care about anything"; 6 = “I have no appetite during the day”; 7 = “I worry about sleeping”; 8 = “I didn’t have enough sleep last night”; 9 = "I am restless"; 10 = "I am tired"; 11 = "It is not effortful to do things"; 12 = “I feel guilty”; 13 = “I am doing things at my normal pace”; 14 = "I feel worthless"; 15 = "I feel that I can't get anything done"; 16 = “I feel that I can’t make decisions”; 17 = "I can't concentrate"; 18 = "I feel hopeless".

Comparing to the afternoon and evening measuring times, the meta-analysis of PHQ-9 score was the most uniform because the associations between PHQ-9 score and all DDI items were significant while the two measuring times only significantly linked to a few DDI items. Heterogeneity in MD symptoms could be seen in the wide range of betas in PHQ-9 score and only some DDI items were significantly associated with the afternoon and evening measuring times.

The momentary ratings of the DDI items significantly predicted by the measuring time were depressed mood, lost interest, fatigue, guilt or worthlessness, and psychomotor symptoms. Among these symptoms, the link between mood and circadian rhythm has been reported (Murray, 2007; Murray et al., 2002). However, slightly inconsistent with Murray's (2007) finding, where only positive affect was associated with circadian rhythm, positive affect was only related to the evening

measuring time in Study 3 but negative affect was linked to both the afternoon and evening measuring times in Study 1. Meta-analysis showed similar results, where positive affect only related to the evening measuring time but the connections between negative affect and the afternoon and evening measuring time were observed.

To sum up, MD severity significantly predicted the momentary ratings of MD symptoms with varying effect on the symptoms while circadian rhythm was only observed in some MD symptoms. MD symptom heterogeneity could be observed in circadian rhythm and between the momentary ratings of MD symptoms and disorder severity.

Limitations and future directions

Previous literature has reported the association between evening chronotype and MD (Kantermann et al., 2012) and MD severity (Au & Reece, 2017). But chronotype was not assessed in the three studies and this had limited the scope of the applicability of the results. Sleep disturbance is another commonly reported MD symptom affected by circadian rhythm (Vadnie & McClung, 2017). But the relationship between the momentary ratings of sleep-related items in the DDI and circadian rhythm was not tested in the three studies because these items were only measured once a day. To dig into the depth of diurnal changes, including assessments of chronotypes, actigraphy monitors, salivary melatonin, and core body temperature would allow a more thorough examination of the influences of diurnal changes on MD symptoms (Robillard et al., 2018).

The next chapter will discuss the relationship between personality and MD severity.

Chapter 5 Personality and MD severity

Introduction

Personality models

Several models were proposed to classify personality traits, among those, the most renowned are the Big Five and the Big Three. The Big Five personality traits compose of openness, conscientiousness, extraversion, agreeableness, and neuroticism (Costa & McCrae, 1985) while the Big Three are negative emotionality, positive emotionality, and disinhibition (Watson & Clark, 1993). Overlaps between the two models have been reported – neuroticism resembles negative emotionality and extraversion coincides positive emotionality, whereas disinhibition in the Big Three inconsistently correlates with conscientiousness and agreeableness in the Big Five (Clark & Watson, 1999). In the current study, the Big Five model was used because most comparable evidences have been collected within this framework and the Big Five has been linked to a wide range of life outcomes (Ozer & Benet-Martínez, 2005; Rammstedt et al., 2017; Roberts et al., 2007).

Facets of personality

The Big Five personality traits are often broken into numerous narrower (or "lower-order") personality traits called facets (Costa & McCrae, 1995). It has been found that facets of the same Big Five traits have at least somewhat distinct etiologies because they are affected by distinct genetic and environmental factors (Jang et al., 2006). They also vary in their links with external variables (e.g., education, diet, or major depression [MD]) (René Mõttus, 2016). For example, depression under neuroticism and cheerfulness under extraversion predicted life satisfaction (Schimmack et al., 2004). Impulsiveness under neuroticism, straightforwardness under agreeableness, and self-discipline under conscientiousness are associated with higher rate of survival in an elderly sample (Weiss & Costa, 2005). Anxiety is linked to the four facets under extraversion and positive emotionality – sociability, positive emotionality, ascendance, and fun-

seeking while MD was only related to positive emotionality (Naragon-Gainey et al., 2009). People with MD are also higher in the facet depression under neuroticism and lower in the facets positive emotion and assertiveness under extraversion (Rector et al., 2012). MD symptoms were associated with the following facets: angry hostility and depression under neuroticism, positive emotions under extraversion, and actions under openness (Chioqueta & Stiles, 2005). Depression and positive emotion or cheerfulness were the facets that consistently predicted MD across several studies.

Normal and abnormal personality traits

Historically and even currently within the medical psychiatric paradigm, pathological or abnormal personality is represented as an expert-agreed set of distinct disorders (DSM-IV, DSM-V) – the categorical model (American Psychiatric Association, 2013a). However, this model of abnormal personality has several problems such as poor convergence between patients' symptoms and the diagnostic categories (a large proportion of patients receive the "waste bin" diagnosis of personality disorder not otherwise specified) and low agreement among diagnosing doctors. To mitigate these problems, there has been a shift towards representing abnormal personality in the same framework as the personality models represent normal personality traits – the dimensional model (Hopwood et al., 2018; Krueger & Tackett, 2003; Trull & Durrett, 2005).

"Normal and abnormal personality are not distinct from one another, and that personality is best represented on a continuum" (Blashfield et al., 2014, p. 38). Normal personality models such as the Big Five have been "explicitly or implicitly assumed to account for both normal and abnormal personality" or, at least, "were developed without explicit attention to any distinction between normal and abnormal personality" (Markon et al., 2005, p. 140). Markon et al. (2005) conducted a meta-analysis and an empirical study. They reported normal and abnormal personality traits shared a hierarchical structure, which mirrored an existing five-factor model of personality traits. Nonetheless, other studies observed an underlying hierarchical model of abnormal personality (Gutierrez et al., 2014;

Widiger & Costa, 2012). Widiger and Costa (2012) suggested a five-factor model while Gutierrez et al. (2014) found a seven-factor model .

Personality disorders and MD

Whether having a personality disorder is related to poor outcome in MD patients is still under debate. Although consensus has yet reached regarding the most prominent types of personality disorder among MD patients, it has been reported that people with MD have a higher probability of having personality disorders than those who do not have MD (Corruble, Ginestet, & Guelfi, 1996; Skodol et al., 1999; Wongpakaran, Wongpakaran, Boonyanaruthee, Pinyopornpanish, & Intaprasert, 2015). Some have reported that early-onset MD was associated with co-occurrence of personality disorder (Alpert et al., 1997; Fava et al., 1996; Ramklint & Ekselius, 2003) but Skodol et al. (1999) did not observe this connection. Shea, Widiger, and Klein (1992) suggested the studies on comorbidity of personality disorder and MD may share a hidden bias because most of the literature has reported that a high percentage of MD patients were also diagnosed with personality disorders. But only a relatively small number of studies found many patients with personality disorders had MD.

Compared to those who only have MD, people who are diagnosed with both personality disorder and MD tend to a have poorer MD treatment outcome (Goddard, Wingrove, & Moran, 2015; Newton-Howes et al., 2013; Newton-Howes, Tyrer, & Johnson, 2006; Shea et al., 1992). However, contesting results of the psychosocial functioning of patients diagnosed with one personality disorder and MD remained unaffected by the diagnoses were reported, while decreased quality of life was found in those having two or more personality disorder and MD (Brieger, Ehrt, Bloeink, & Marneros, 2002). A randomized control trial showed MD patients with personality disorders did not have negative outcome in MD treatment (Kool et al., 2005).

Personality and MD

Personality traits relate differently to MD and the associations between trait neuroticism and MD has often been reported. Several studies found neuroticism has been repeatedly reported to be associated with the onset of MD (Kendler et al., 2004), the recurrence of MD (Burcusa & Iacono, 2007), and the risk of lifetime MD (Xia et al., 2011). Noteboom, Beekman, Vogelzangs, and Penninx (2016) observed negative associations between new MD episodes and extraversion, agreeableness, and conscientiousness. But clinical conditions were more prominent and as a result, some of these associations disappeared after controlling for MD severity and life-time prevalence of anxiety disorder. Only neuroticism remains a significant predictor of new MD episodes independent of the two disorder characteristics mentioned above. A study of first- and second-year undergraduate students found stress was the mediating factor between personality and MD (Kuznetsova, Knyazev, Dorosheva, Bocharov, & Savostyanov, 2016). The associations between MD and three personality traits – neuroticism, extraversion, and conscientiousness - were reported. Neuroticism predicted MD and those who had MD were relatively low in extraversion scores. A review article observed the associations between MD and neuroticism, extraversion, and conscientiousness (Klein et al., 2011). Chioqueta and Stiles (2005) reported MD symptoms were positively related to neuroticism and openness and negatively predicted by extraversion.

"Concurrent associations" between personality traits in both the Big Five and the Big Three Models and mental disorders including MD, anxiety disorder, and substance use disorder were reported in a review of 66 meta-analyses covering 175 cross-sectional studies (Kotov et al., 2010, p. 803). They found high level of neuroticism, low level of conscientiousness, and low extraversion were highly related to the three mental disorders. Disinhibition was related with some of the disorders – unipolar MD, dysthymic disorder, anxiety disorder, and substance use disorder. Agreeableness was only linked to substance use disorder. No associations between openness and the mental disorders were found. Different associations between personality traits and mental disorders may be explained by an unbalanced personality hierarchy, where elements at the same level of hierarchy

have divergent levels of abstraction (Markon et al., 2005). The level of abstraction is used to describe objects in a hierarchy, where objects at the same level of hierarchy provide identical amount of details. Markon et al. (2005) suggested the level of abstraction of neuroticism might be different from the other traits. The divergent levels of abstraction may explain the correlations between personality traits and mental disorders. Kotov et al. (2010) further tested the correlations between the Big Five personality traits using data from Markon et al. (2005). They also controlled for neuroticism to remove the correlations between the personality traits and mental disorders explained by associations between neuroticism and other personality traits. Their results showed decreases in effect sizes of conscientiousness, disinhibition, and extraversion but the effects of openness remained the same.

Several possible mechanisms underlying the association between neuroticism and MD have been reported (Nagel, Jansen, et al., 2018; Nagel, Watanabe, et al., 2018; Shirata et al., 2018). The genetic correlations between facets under neuroticism showed they were genetically heterogeneous but a subsequent hierarchical clustering analysis found two genetically homogeneous clusters – depressed affect and worry (Nagel, Watanabe, et al., 2018). A meta-analysis of genome-wide association studies of 449,484 people and 14,978,477 SNPs identified some neuroticism-related genetic variants (124 new loci out of the 136 identified loci) and enrichment of genes (gene expression or protein production) related to neuroticism in some brain regions, cell types, and pathways (Nagel, Jansen, et al., 2018). Considerable genetic correlations between neuroticism and MD and two facets under neuroticism – depressed affect and worry were reported, too.

The role of epigenetic modifications in MD was highlighted in a review (Dalton et al., 2014). Epigenetic modifications alter DNA expression without changing the DNA sequence (A. D. Goldberg et al., 2007). Epigenetic mechanisms include DNA methylation, covalent chromatin modification, noncovalent chromatin modification, and noncoding RNA. Some epigenetic modifications are heritable and

some are reversible. Both animal and human studies have found that epigenetics may explain the influences of environmental factors such as early adverse life events on later MD episodes (Dalton et al., 2014).

Models explaining the relationships between personality and MD

Several models were proposed to explain the association between personality and MD (Bagby et al., 2008; Klein et al., 2011). These models were constructed based on the causal relationship between personality and MD – they share a common cause, MD causally affects personality, personality has a causal influence on MD, and there was a continuum spanning from subclinical personality trait, subclinical MD symptoms, and MD.

The studies

Based on the literature, there are the associations between high neuroticism, low conscientiousness, or low extraversion and MD, this chapter will test the links between high neuroticism, low conscientiousness, or low extraversion and MD severity (H12). Since the facets of the Big Five were measured, we test another hypothesis to link the facets to MD – depression under neuroticism and cheerfulness under extraversion predict MD severity (H13). To explore the associations between personality and different aspects of MD measures, the relationships between personality traits and facets and momentary MD ratings and MD symptom variability were tested, too. In three studies, we used a retrospective MD questionnaire, Patient Health Questionnaire-9 (PHQ-9) to measure MD severity, and a momentary MD questionnaire, Daily Depression Items (DDI), to measure momentary MD ratings. MD severity, the momentary MD ratings, and the MD symptom variability were tested using the sums of the PHQ-9, the means of the DDI ratings, and the standard deviations of the DDI ratings, respectively. The relationships between personality traits and facets and the items in the PHQ-9 and the DDI are tested to observe the symptom dynamics: if the associations between different MD symptoms and personality characteristics are similar, this is consistent with MD being etiologically homogeneous, whereas mixed association patterns are consistent with the reverse.

Materials and Method

The participants, materials, and procedure in the three studies were the same as those described in Studies 1, 2, and 3 in Materials and Method in Chapters 2–4.

Results

The 120-item International Personality Item Pool was employed to measure personality traits. However, items measuring the same traits or facets were not randomly interspersed in the questionnaires. The reversed-scoring items were adjusted before calculating the score for each traits and facets.

Regression was used to analyze the relationships between personality traits, facets, and MD severity. The R code of the model could be found in Appendix B. The controlling variables were the demographic variables – age, gender, educational attainment, marital status, and employment status. Educational attainment was treated as a continuous variable because the options in this question follows a chronological order. The same as Chapters 2, 3, and 4, marital status and employment status were collapsed into two levels. In marital status, one level included those who were single, divorced, or widowed and the other level comprised people who were married or in a relationship. In employment status, employed or self-employed and full-time student were in one level and part-time employed, retired, and unemployed were in the other level. The sum of the retrospective MD questionnaire, the PHQ-9 was used as a measure of MD severity. The relationships between the PHQ-9 items and personality traits or facets were tested separately to see how each MD symptom related to personality traits. For each DDI item, the means and the standard deviations of the momentary ratings were calculated and they represented the momentary MD symptom ratings and variability of MD symptoms, respectively. In tables, the results were presented as items mapped across the three studies. Due to the restriction of page size, items not measured in the studies were not shown in the respective tables.

In regression models, one of the personality traits or facets and all controlling variables were the independent variables. The dependent variable was one of the following – the sums of the PHQ-9, each PHQ-9 item, the mean momentary rating of each DDI item, or the standard deviation of the momentary ratings of each DDI item. The *p*-values were adjusted using false discovery rate (FDR) to take care of the issue of multiple comparison. The same analyses were used to analyze three different sets of data from the three studies. The results of the three studies were presented below. To observe whether there were consistent trends or patterns in the findings, replicability of the three studies were assessed, too. This was followed by a meta-analysis to provide more robust findings.

Study 1

The results supported the hypothesis of high neuroticism, low extraversion, and low conscientiousness significantly predicted MD severity (Table 5.1). Openness and agreeableness were not significant predictors of PHQ-9 scores. The hypothesis of depression (N3) under neuroticism and cheerfulness (E6) under extraversion predicted MD severity was supported as well. MD severity was also significantly and positively predicted by other facets including N1 anxiety, N4 self-consciousness, N5 immoderation, and N6 vulnerability and significantly and negatively predicted by facets including E1 friendliness, E2 gregariousness, O4 adventurousness, O6 liberalism, C1 self-efficacy, and C5 self-discipline negatively predicted MD severity. Even though agreeableness did not significantly predict MD severity, A1 trust significantly and negatively and A5 modesty significantly and positively predicted MD severity. Therefore, the associations between MD severity and personality were at least to some extent driven by facets rather than the Big Five traits.

High neuroticism significantly predicted the scores of all PHQ-9 items. Low extraversion and low conscientiousness significantly predicted nearly all PHQ-9 items. The facets N1 anxiety, N3 depression, and N6 vulnerability under neuroticism and E6 cheerfulness under extraversion significantly predicted all PHQ-9 items.

Some facets significantly predicted some of the PHQ-9 items. Openness and agreeableness did not significantly predicted any PHQ-9 items.

Overall, all of the mean momentary ratings of the DDI items were significantly predicted by high neuroticism and majority of the mean ratings were predicted by low extraversion and low conscientiousness (Table 5.2). No significant relationships between openness and agreeableness and the mean momentary ratings were found. The results of the facets showed slightly greater variances compared to those of the traits. Depression and cheerfulness significantly predicted nearly all of the mean momentary ratings. N1 anxiety significantly predicted the mean momentary ratings. Some facets significantly related to the mean momentary ratings of none or some DDI items.

The variabilities of most DDI items was significantly predicted by neuroticism and some by conscientiousness (Table 5.3). There were significant relationships between N3 depression and the variability of some DDI items but E6 cheerfulness was only significantly associated with the variability of two DDI items. Other facets including several in openness and agreeableness were found to be significantly related to the variability of DDI items, too. But the number of significant associations was smaller compared to those in the mean momentary DDI ratings.

Neuroticism and conscientiousness and the facets depression and anxiety consistently and significantly predicted MD severity, momentary MD ratings, and MD symptom variability. Sparingly significant associations were observed in other traits and facets. The PHQ-9 and DDI items related differently with personality traits and facets may imply heterogeneity in MD symptoms.

Two more studies were conducted to test the findings in Study 1.

Table 5.1 *Standardized betas of the Big Five personality traits and facets extract from the regression models testing the relationships between personality traits and facets and the PHQ-9 items in Study 1*

	PHQ-9	1	2	3	4	5	6	7	8	9
N	.70***	.54***	.60***	.57***	.54***	.42***	.63***	.55***	.46***	.45***
E	-.41***	-.40***	-.43***	-.26*	-.24*	-.20	-.45***	-.24*	-.23	-.42***
O	.02	-.02	.02	-.02	.02	-.02	-.09	.13	.10	.06
A	.02	.02	.02	-.03	.13	.01	-.01	.02	-.04	-.03
C	-.37***	-.31**	-.29*	-.25	-.25*	-.17	-.39***	-.38***	-.32**	-.21
N1	.58***	.36***	.49***	.54***	.44***	.31**	.57***	.41***	.46***	.38***
N2	.26*	.13	.21	.22	.18	.18	.21	.29*	.22	.17
N3	.65***	.56***	.62***	.45***	.44***	.37***	.59***	.54***	.45***	.48***
N4	.42***	.41***	.36***	.38***	.32***	.21	.38***	.32**	.17	.29*
N5	.37***	.31**	.26*	.36***	.35***	.33***	.31**	.21	.16	.14
N6	.52***	.36***	.46***	.36***	.45***	.31**	.48***	.42***	.39***	.32**
E1	-.40***	-.42***	-.39***	-.30**	-.18	-.19	-.39***	-.28*	-.28*	-.35***
E2	-.39***	-.30**	-.40***	-.31**	-.26*	-.18	-.42***	-.27*	-.21	-.34***
E3	-.16	-.21	-.17	-.09	-.20	-.10	-.13	-.06	-.02	-.11
E4	-.06	-.18	-.15	.07	.00	.15	-.15	.02	-.10	-.16
E5	-.16	-.13	-.16	-.08	-.07	-.13	-.27*	-.07	.02	-.25
E6	-.49***	-.39***	-.46***	-.34***	-.25*	-.32***	-.49***	-.31**	-.34***	-.50***
O1	-.02	-.16	-.02	.02	-.06	-.07	-.08	.12	.07	.07
O2	.06	.02	.06	.01	.06	.00	-.06	.09	.11	.19
O3	.14	.17	.17	.10	.17	.07	.08	.07	.03	.06
O4	-.25*	-.24*	-.29**	-.23	-.20	-.10	-.25*	-.06	-.05	-.30**
O5	-.08	-.06	-.01	-.13	-.09	-.11	-.12	-.01	-.03	.02
O6	.30**	.32***	.23	.19	.25*	.19	.18	.26*	.22	.20
A1	-.36***	-.28*	-.35***	-.33***	-.23*	-.21	-.32***	-.24*	-.23	-.30**
A2	-.08	-.13	-.08	-.07	.01	-.05	-.04	-.05	-.09	-.10
A3	.05	.08	.12	-.05	.15	.00	.01	.03	-.03	.03
A4	.03	.08	.00	.04	.11	.04	.03	-.05	-.04	.00
A5	.28**	.23	.26*	.20	.24*	.22	.27*	.24*	.11	.12
A6	.11	.07	.11	.09	.17	.01	-.01	.12	.12	.15
C1	-.36***	-.32***	-.30**	-.18	-.21	-.25*	-.40***	-.25*	-.26*	-.35***
C2	-.18	-.10	-.17	-.22	-.19	-.09	-.21	-.16	-.04	.03
C3	-.22	-.13	-.15	-.17	-.09	-.14	-.15	-.24*	-.29*	-.23
C4	-.17	-.21	-.16	-.03	-.02	-.08	-.16	-.19	-.19	-.23
C5	-.42***	-.42***	-.30**	-.25*	-.34***	-.15	-.46***	-.34***	-.37***	-.27*
C6	-.08	-.04	-.02	-.06	-.05	.04	-.10	-.22	-.12	.08

Note. PHQ-9 = PHQ-9 total score; 1–9 = PHQ-9 items; 1 = little interest; 2 = feeling down; 3 = trouble sleeping; 4 = tired; 5 = altered appetite; 6 = feeling bad about self; 7 = concentration problem; 8 = psychomotor changes; 9 = suicidal ideation; N = neuroticism; E = extraversion; O = openness; A = agreeableness; C = conscientiousness; N1 = anxiety; N2 = anger; N3 = depression; N4 = self-consciousness; N5 = immoderation; N6 = vulnerability; E1 = friendliness; E2 = gregariousness; E3 = assertiveness; E4 = activity level; E5 = excitement-seeking; E6 = cheerfulness; O1 = imagination; O2 = artistic interests; O3 = emotionality; O4 = adventurousness; O5 = intellect; O6 = liberalism; A1 = trust; A2 = morality; A3 = altruism; A4 = cooperation; A5 = modesty; A6 = sympathy; C1 = self-efficacy; C2 = orderliness; C3 = dutifulness; C4 = achievement-striving,; C5 = self-discipline; C6 = cautiousness. * p < .05. ** p < .01. *** p < .001.

Table 5.2 *Standardized betas of the Big Five personality traits and facets in regression models testing the relationships between personality traits and facets and the mean momentary ratings of the DDI items in Study 1*

	2	3	4	5	6	7	8	9
N	.52***	.52***	.56***	.40***	.34***	.49***	.43***	.45***
E	-.49***	-.46***	-.44***	-.42***	-.18	-.34***	-.20	-.23
O	.01	.04	.01	-.11	-.02	.01	.12	.13
A	-.12	-.03	-.09	-.13	-.07	-.09	.00	-.08
C	-.31**	-.33***	-.31**	-.30**	-.18	-.25*	-.32***	-.22
N1	.45***	.46***	.49***	.27*	.30**	.48***	.40***	.45***
N2	.18	.17	.20	.11	.13	.18	.17	.21
N3	.54***	.57***	.53***	.42***	.29**	.39***	.35***	.38***
N4	.33***	.32***	.35***	.28**	.20	.32***	.24*	.27*
N5	.17	.16	.21	.19	.16	.18	.31***	.06
N6	.40***	.38***	.43***	.30**	.28*	.42***	.28**	.44***
E1	-.49***	-.50***	-.49***	-.48***	-.25*	-.37***	-.21	-.25*
E2	-.45***	-.42***	-.40***	-.25*	-.10	-.31***	-.22	-.24*
E3	-.12	-.05	-.10	-.20	-.11	-.15	-.06	-.07
E4	-.16	-.17	-.10	-.28*	-.02	-.03	.04	.02
E5	-.23	-.21	-.18	-.08	-.02	-.11	-.05	-.08
E6	-.53***	-.53***	-.52***	-.44***	-.23*	-.40***	-.29**	-.32***
O1	.01	.05	.01	-.09	-.02	.13	.20	.22
O2	.06	.06	.06	-.01	-.04	.00	.04	.06
O3	-.04	.01	-.03	-.09	.11	.07	.09	.10
O4	-.23	-.20	-.21	-.17	-.11	-.24*	-.09	-.17
O5	.05	.01	.01	-.14	-.11	-.09	.00	.04
O6	.23	.26*	.23	.18	.14	.20	.19	.23
A1	-.36***	-.38***	-.36***	-.28*	-.26*	-.35***	-.24*	-.21
A2	-.15	-.11	-.16	-.18	-.10	-.11	-.04	-.14
A3	-.06	.02	-.05	-.15	.01	-.06	.00	.03
A4	-.01	.04	.01	-.02	.02	.08	.01	-.03
A5	.16	.25*	.18	.17	.08	.16	.18	.03
A6	.02	.09	.05	-.01	.03	-.04	.08	.06
C1	-.32***	-.30***	-.29**	-.17	-.06	-.35***	-.21	-.14
C2	-.13	-.15	-.14	-.18	-.10	-.05	-.24*	-.10
C3	-.19	-.15	-.15	-.08	-.13	-.14	-.06	-.16
C4	-.16	-.19	-.14	-.32***	-.05	-.06	-.12	-.05
C5	-.45***	-.44***	-.46***	-.33***	-.15	-.29*	-.41***	-.32**
C6	.01	-.05	-.03	-.05	-.14	-.07	-.11	-.07

	10	11	14	15	17	18	19
N	.51***	.24*	.64***	.60***	.59***	.63***	.51***
E	-.29**	-.09	-.50***	-.36***	-.30***	-.48***	-.44***
O	.08	.11	-.02	.12	.13	.01	.01
A	.04	.01	-.05	.00	-.03	-.07	-.06
C	-.31***	-.12	-.32***	-.43***	-.36***	-.31**	-.30**
N1	.44***	.25*	.53***	.45***	.49***	.53***	.48***
N2	.15	.08	.22	.28*	.29**	.22	.14
N3	.46***	.21	.66***	.52***	.47***	.64***	.51***
N4	.36***	.17	.38***	.43***	.41***	.38***	.29**
N5	.24*	.03	.22	.28*	.26*	.23	.22
N6	.39***	.22	.53***	.44***	.44***	.50***	.38***
E1	-.30***	-.08	-.48***	-.40***	-.37***	-.50***	-.47***
E2	-.33***	-.14	-.44***	-.32***	-.29**	-.41***	-.34***
E3	-.08	.06	-.18	-.18	-.12	-.10	-.05
E4	-.02	.03	-.24*	-.17	-.06	-.15	-.22
E5	-.08	-.11	-.18	-.08	-.05	-.20	-.20
E6	-.34***	-.09	-.53***	-.32***	-.31***	-.57***	-.52***
O1	.17	.11	.08	.16	.24*	.05	-.02
O2	-.01	.05	.03	.08	.05	.02	.05
O3	.11	.14	.04	.05	.06	.05	.04
O4	-.14	-.04	-.32***	-.15	-.10	-.27*	-.23*
O5	-.03	-.03	-.07	-.01	-.02	-.02	.04
O6	.22	.18	.22	.31***	.24*	.28*	.23
A1	-.22*	-.05	-.28**	-.21	-.31***	-.32***	-.31***
A2	-.06	-.08	-.15	-.13	-.12	-.18	-.17
A3	.11	.06	-.04	.06	.00	-.04	.02
A4	.00	-.04	-.01	-.03	-.01	-.01	.01
A5	.24*	.08	.22	.17	.21	.19	.16
A6	.07	.04	.05	.15	.12	.11	.08
C1	-.18	-.13	-.31***	-.25*	-.20	-.30**	-.29**
C2	-.22*	-.10	-.13	-.25*	-.20	-.15	-.13
C3	-.07	.01	-.12	-.11	-.10	-.15	-.15
C4	-.11	.02	-.22	-.27*	-.17	-.19	-.17
C5	-.39***	-.21	-.44***	-.48***	-.40***	-.43***	-.43**
C6	-.14	-.02	-.04	-.21	-.23*	.00	.00

Note. N = neuroticism; E = extraversion; O = openness; A = agreeableness; C = conscientiousness; N1 – C6 = the facets; 1–20 represent items in the DDI; 1 = I feel happy; 2 = I feel sad; 3 = I feel irritable; 4 = I enjoy what I am doing; 5 = I don't care about anything; 6 = I have no appetite during the day; 7 = I worry about sleeping; 8 = I didn't have enough sleep last night; 9 = I am rest less; 10 = I am tired; 11= It is not effortful to do things; 12 = I feel guilty; 13 = I am doing things at my normal pace; 14 = I feel worthless; 15 = I feel that I can't get anything done; 16 = I feel that I can't make decisions; 17 = I can't concentrate; 18 = I feel hopeless; 19 = How's your day; 20 = How would you rate your overall physical health today. There were revisions of the DDI over the course of the three studies and items 1, 12, 13, 16, and 20 were not included in Study 1. * $p < .05$. ** $p < .01$. *** $p < .001$.

Table 5.3 *Standardized betas of the Big Five personality traits and facets in regression models testing the relationships between personality traits and facets and the variabilities of the DDI items in Study 1*

	2	3	4	5	6	7	8	9
N	.42***	.29*	.38***	.45***	.42***	.24	.17	.37***
E	-.10	.01	-.13	-.09	-.20	.03	.02	-.06
O	.14	.18	.10	.08	-.05	-.01	.14	.07
A	.11	.21	.14	.08	.09	.00	.12	.08
C	-.25*	-.24*	-.22	-.28*	-.23	-.20	-.21	-.22
N1	.39***	.28*	.35***	.44***	.38***	.29*	.21	.35***
N2	.22	.19	.14	.20	.10	.10	.02	.16
N3	.29**	.19	.28**	.38***	.32**	.05	.08	.22
N4	.24*	.13	.23*	.19	.29**	.09	.11	.25*
N5	.28*	.25*	.30**	.26*	.28*	.21	.16	.25*
N6	.30**	.15	.26*	.34***	.34***	.26*	.14	.28*
E1	-.15	-.07	-.22*	-.21	-.22	-.05	-.04	-.15
E2	-.13	-.01	-.13	-.07	-.10	.05	.01	-.09
E3	-.05	.00	-.05	.05	-.23	-.02	-.01	-.08
E4	.03	.04	.07	.09	-.05	.12	.13	.15
E5	.09	.15	.03	.07	.01	.09	.10	.05
E6	-.17	-.05	-.21	-.26*	-.23	-.06	-.08	-.11
O1	.16	.17	.04	.09	.06	.05	.03	.13
O2	.03	.06	.08	-.01	-.04	-.04	.05	.02
O3	.20	.21	.13	.20	.22	.14	.25*	.03
O4	.01	.13	.01	-.04	-.23	.03	.06	.02
O5	.02	-.06	.03	-.02	-.21	-.10	.01	-.05
O6	.05	.11	.08	.09	.05	-.13	.12	.10
A1	-.18	-.10	-.25*	-.21	-.10	-.05	-.06	-.07
A2	-.06	.03	-.01	-.08	-.08	-.09	-.01	-.02
A3	.24*	.34***	.20	.16	.12	.05	.16	.14
A4	-.02	.01	.06	-.03	.03	.00	.00	-.02
A5	.22	.25*	.26*	.24*	.17	.03	.16	.11
A6	.18	.22	.22	.20	.16	.06	.17	.14
C1	-.20	-.11	-.20	-.19	-.28*	-.19	-.18	-.15
C2	-.09	-.09	-.07	-.10	-.01	-.04	-.05	-.10
C3	-.07	-.04	-.02	-.11	-.05	-.08	-.19	-.06
C4	-.10	-.08	-.07	-.17	-.17	-.02	.01	-.04
C5	-.29*	-.22	-.30**	-.28*	-.30*	-.25*	-.21	-.30**
C6	-.18	-.28*	-.14	-.19	-.11	-.14	-.17	-.16

	10	11	14	15	17	18	19
N	.00	.06	.47***	.34***	.40***	.49***	.35***
E	.17	.11	-.14	-.03	-.10	-.14	-.06
O	.14	.09	.10	.22	.09	.17	.12
A	.10	.13	.07	.11	.10	.09	.10
C	-.15	-.06	-.27*	-.25*	-.24*	-.30**	-.17
N1	.03	.09	.45***	.31***	.37***	.45***	.38***
N2	.02	.05	.22	.15	.15	.18	.14
N3	-.11	-.07	.34***	.27**	.30**	.41***	.25*
N4	-.01	.03	.22	.15	.21	.25*	.15
N5	.11	.19	.31**	.31***	.34***	.35***	.33***
N6	.00	.02	.37***	.19	.28*	.36***	.21
E1	.10	.02	-.16	-.11	-.15	-.22*	-.13
E2	.14	.14	-.13	-.05	-.13	-.09	-.04
E3	.01	-.03	-.10	.01	-.07	-.02	-.01
E4	.08	.07	-.04	.13	.07	.03	.04
E5	.18	.20	.01	.06	.03	.02	.10
E6	.17	.08	-.18	-.13	-.16	-.27*	-.16
O1	.10	.03	.11	.11	.08	.13	.11
O2	.07	.01	.03	.12	.05	.06	-.02
O3	.11	.15	.18	.23*	.21	.22	.20
O4	.20	.11	-.04	.05	-.11	-.03	.00
O5	.02	.04	-.04	.09	-.02	.08	.00
O6	-.06	-.05	.12	.18	.12	.15	.12
A1	.07	.04	-.12	-.16	-.13	-.19	-.19
A2	.04	.07	-.02	-.03	.03	-.05	-.02
A3	.16	.24*	.19	.24*	.17	.20	.22
A4	.00	.01	-.09	-.07	-.01	-.04	.00
A5	.06	.00	.15	.14	.15	.19	.19
A6	.03	.13	.16	.26*	.16	.22	.15
C1	-.03	.04	-.19	-.09	-.14	-.20	-.19
C2	-.05	.02	-.11	-.10	-.10	-.19	-.05
C3	-.10	-.09	-.05	-.12	-.06	-.06	.02
C4	-.05	-.02	-.09	-.09	-.07	-.13	-.06
C5	-.05	-.01	-.26*	-.27*	-.30**	-.35***	-.25*
C6	-.23	-.15	-.22	-.20	-.18	-.14	-.08

Note. N = neuroticism; E = extraversion; O = openness; A = agreeableness; C = conscientiousness; N1 – C6 = the facets; 1–20 represent items in the DDI; 1 = I feel happy; 2 = I feel sad; 3 = I feel irritable; 4 = I enjoy what I am doing; 5 = I don't care about anything; 6 = I have no appetite during the day; 7 = I worry about sleeping; 8 = I didn't have enough sleep last night; 9 = I am rest less; 10 = I am tired; 11= It is not effortful to do things; 12 = I feel guilty; 13 = I am doing things at my normal pace; 14 = I feel worthless; 15 = I feel that I can't get anything done; 16 = I feel that I can't make decisions; 17 = I can't concentrate; 18 = I feel hopeless; 19 = How's your day; 20 = How would you rate your overall physical health today. There were revisions of the DDI over the course of the three studies and items 1, 12, 13, 16, and 20 were not included in Study 1. * $p < .05$. ** $p < .01$. *** $p < .001$.

Study 2

Only neuroticism but not extraversion and conscientiousness significantly predicted MD severity and H12 was partially supported (Table 5.4). The facets depression under neuroticism and cheerfulness under extraversion were both significantly linked to MD severity. H13 was supported. Two facets under neuroticism – N1 anxiety and N6 vulnerability – were significant predictors of MD severity, too. Neuroticism together with the facets anxiety, depression, vulnerability, and cheerfulness were significant predictors of the scores of several PHQ-9 items.

For the mean momentary MD ratings, only neuroticism and extraversion significantly predicted the mean momentary ratings of seven and two items in the DDI, respectively (Table 5.5). The following facets – N1 anxiety, N3 depression, N6 vulnerability, and E6 cheerfulness - were significant predictors of the mean momentary ratings of some DDI items. The variabilities of a few MD symptoms were significantly predicted by extraversion and several facets (Table 5.6).

The results of Study 2 were not totally consistent with those in Study 1 because H12 of MD severity were predicted by high neuroticism, low extraversion, and low conscientiousness was only partially supported in Study 2. The divergent and sometimes limited links between personality traits and facets and the items in the PHQ-9 and the DDI may indicate MD symptoms are heterogeneous.

One last study was conducted to verify the findings in Studies 2 and 3.

Table 5.4 *Standardized betas of the Big Five personality traits and facets in regression models testing the relationships between personality traits and facets and the PHQ-9 items in Study 2*

	PHQ-9	1	2	3	4	5	6	7	8	9
N	.42**	.36*	.41**	.38*	.35*	.16	.57***	.09	.07	.33
E	-.13	-.18	-.26	-.10	-.05	.05	-.27	.09	.01	-.20
O	.18	.06	.06	.16	.12	.29	.06	.17	.08	.09
A	.24	.21	.21	.17*	.36	.10	.10	.13	.01	.22
C	-.03	.03	.10	-.11	-.04	-.04	-.21	-.09	.13	.08
N1	.49***	.48***	.45***	.45***	.39**	.16	.52***	.24	.19	.27
N2	.20	.07	.12	.24	.19	.09	.39*	.04	-.02	.14
N3	.46***	.36*	.49***	.37*	.40**	.16	.53***	.15	.16	.37*
N4	.18	.12	.25	.11	.16	.02	.43***	-.09	-.09	.26
N5	.01	.11	-.06	.06	-.04	.10	.07	-.07	-.16	.00
N6	.47***	.40*	.52***	.43*	.37*	.15	.45**	.15	.27	.36
E1	-.19	-.10	-.27	-.14	-.10	-.10	-.32	.02	.01	-.25
E2	-.03	.03	-.01	-.09	.00	.01	-.10	.10	-.06	-.08
E3	.06	-.04	.03	.03	.06	.14	-.04	.07	.16	-.04
E4	.03	-.07	-.14	.14	.09	.19	-.06	.06	-.01	-.10
E5	-.05	-.12	-.18	-.10	-.13	.17	-.12	.10	.06	-.05
E6	-.35*	-.42**	-.49***	-.21	-.12	-.21	-.40**	-.03	-.15	-.26
O1	-.05	-.20	-.12	.01	-.04	.07	-.11	-.03	.03	.03
O2	.22	.09	.07	.30	.12	.20	.10	.18	.14	.17
O3	.12	.07	.08	.16	.07	.08	-.02	.13	.02	.18
O4	-.02	-.05	-.11	-.16	.05	.29	-.16	.10	-.01	-.16
O5	.20	.07	.23	.07	.04	.25	.19	.18	.11	.09
O6	.19	.19	.11	.11	.10	.23	.20	.13	.02	.06
A1	-.16	-.11	-.19	-.24	.00	-.14	-.16	-.06	-.09	.00
A2	.12	.11	.21	.11	.22	.03	-.01	.01	.04	.05
A3	.31	.21	.24	.33	.36*	.25	.14	.23	-.01	.20
A4	.31	.22	.30	.17	.39*	.20	.14	.21	.13	.23
A5	.33	.38*	.24	.27	.41*	.07	.21	.16	.10	.34
A6	.19	.10	.22	.19	.27	.10	.13	.03	-.02	.17
C1	-.19	-.15	-.10	-.22	-.19	-.03	-.13	.00	-.21	-.26
C2	-.04	-.10	.02	.07	-.02	-.10	-.15	-.19	.07	.21
C3	-.02	.02	.09	-.01	.06	.00	-.10	-.12	-.01	-.09
C4	.12	.12	.17	.07	.10	.22	-.01	.05	-.01	.04
C5	-.09	-.15	-.03	-.04	-.09	.05	-.26	-.12	.04	-.01
C6	.00	.14	.11	-.18	-.03	-.08	-.16	-.01	.23	.11

Note. PHQ-9 = PHQ-9 total score; 1–9 = items in the PHQ-9; N = neuroticism; E = extraversion; O = openness; A = agreeableness; C = conscientiousness; N1 – C6 = the facets. * $p < .05$. ** $p < .01$. *** $p < .001$.

Table 5.5 *Standardized betas of the Big Five personality traits and facets in regression models testing the relationships between personality traits and facets and the mean momentary ratings of the DDI items in Study 2*

	2	3	4	5	6	7	8	9	10
N	.35*	.34*	.16	.19	.03	.18	.36*	.12	.38*
E	-.35*	-.17	-.15	-.24	.01	-.04	-.09	-.04	-.04
O	.02	.01	.07	-.11	.26	.10	.05	.24	-.03
A	-.13	-.07	-.03	-.16	-.10	.02	.20	.04	.20
C	-.05	-.17	-.03	-.16	-.06	-.11	-.18	-.13	-.10
N1	.50***	.44***	.43***	.30*	.21	.17	.29	.31	.35*
N2	.01	.16	-.14	.08	-.12	.04	.06	.04	.16
N3	.34*	.28	.08	.15	.01	.24	.47***	.11	.48***
N4	.13	.05	.07	.04	-.07	-.02	.21	-.08	.16
N5	.19	.15	.15	.07	-.08	.12	.23	-.03	.20
N6	.34	.39**	.05	.19	.21	.22	.27	.17	.25
E1	-.19	-.05	.02	-.10	.01	-.05	-.02	-.01	.09
E2	-.21	-.01	-.08	.01	-.03	-.02	-.12	-.07	-.12
E3	-.03	-.01	.07	-.22	.19	.04	-.06	.09	-.04
E4	-.16	-.17	.04	-.25	.08	.13	.06	.04	.15
E5	-.19	-.04	-.18	-.06	.07	-.04	-.05	.02	-.11
E6	-.60***	-.42***	-.43***	-.33*	-.30	-.20	-.13	-.23	-.09
O1	-.15	-.09	-.05	-.09	-.06	-.03	-.05	.18	-.09
O2	.04	.05	.01	.00	.26	.19	-.01	.14	-.05
O3	.01	.05	.04	-.13	.02	-.11	.06	.20	.09
O4	-.17	-.08	-.09	-.24	.21	.02	.07	.08	-.03
O5	.11	.01	.05	-.09	.28	-.04	-.16	.05	-.28
O6	.21	.10	.25	.13	.26	.15	.10	.27	.08
A1	-.17	-.17	-.06	-.26	-.20	-.23	.07	-.10	.14
A2	-.17	-.11	-.09	-.23	-.03	-.06	.20	.00	.12
A3	-.10	.01	-.04	-.14	-.03	-.03	.13	.08	.17
A4	-.22	-.18	-.11	-.18	.00	.10	.26	-.08	.18
A5	-.02	.05	-.05	.08	-.07	.09	.28	-.01	.21
A6	-.02	.01	.10	-.09	-.01	.06	-.05	.20	.06
C1	-.14	-.16	-.04	-.26	.00	-.17	-.09	-.11	-.04
C2	.00	-.02	-.09	-.02	-.10	.12	-.06	-.13	-.09
C3	.09	.00	.12	-.07	.01	.04	.10	.05	.06
C4	.01	-.06	.13	-.25	.15	.08	.12	-.03	.07
C5	-.08	-.12	-.17	-.25	.07	.04	-.16	-.10	-.08
C6	-.07	-.18	-.05	-.02	-.10	-.24	-.23	-.14	-.12

	11	13	14	15	17	18	19	20
N	.36*	-.05	.19	.45***	.45***	.24	.07	.25
E	-.32	.34	-.11	-.35*	-.28	-.11	-.19	-.12
O	-.09	.23	.13	-.07	-.08	.19	.17	.12
A	-.04	.12	-.01	.02	.08	.01	-.17	-.01
C	-.03	.04	-.17	-.19	-.20	-.14	-.04	-.24
N1	.35*	-.02	.35*	.44***	.41**	.43***	.27	.22
N2	.09	.17	.07	.20	.27	.06	-.22	.15
N3	.32	-.11	.19	.45***	.44***	.21	.08	.32
N4	.22	-.19	.06	.27	.25	.05	.10	.04
N5	.21	.07	-.05	.18	.21	.02	.02	.09
N6	.30	-.12	.23	.37*	.33	.26	.03	.26
E1	-.24	.24	-.09	-.15	-.14	-.04	-.09	-.09
E2	-.25	.26	-.01	-.15	-.14	.03	-.17	.02
E3	-.06	.13	.03	-.14	-.13	.06	.05	-.07
E4	-.09	.19	-.04	-.21	-.17	-.03	.04	-.15
E5	-.22	.26	-.04	-.20	-.14	-.07	-.19	.11
E6	-.36*	.26	-.29	-.53***	-.39*	-.38**	-.38**	-.32
O1	-.01	.28	-.03	-.07	.01	-.01	-.04	.06
O2	.06	.20	.10	.01	.04	.18	.09	.18
O3	-.09	.11	.09	.02	.01	.10	.04	-.05
O4	-.21	.22	.01	-.27	-.26	-.01	.02	.16
O5	-.18	.15	.15	-.07	-.21	.18	.15	.01
O6	-.04	-.04	.17	.26	.21	.27	.28	.11
A1	-.11	.02	-.13	-.17	-.11	-.20	-.16	-.26
A2	-.14	-.07	-.12	.00	.04	-.07	-.09	-.07
A3	-.07	.22	.02	.02	.08	.09	-.13	-.01
A4	-.17	.09	-.01	-.13	-.16	-.03	-.09	-.11
A5	.12	-.07	.08	.25	.27	.10	-.05	.32
A6	.12	.21	.05	.04	.11	.14	-.05	-.01
C1	-.26	.24	-.10	-.26	-.26	-.11	-.05	-.27
C2	.15	-.16	-.20	-.22	-.16	-.14	-.11	-.15
C3	.02	-.09	-.02	.02	-.05	-.02	.04	.11
C4	-.05	.04	.00	-.07	-.15	.00	.00	.03
C5	-.01	.10	-.13	-.34	-.32	-.17	-.04	-.14
C6	-.04	.04	-.14	-.04	-.05	-.12	.00	-.24

Note. N = neuroticism; E = extraversion; O = openness; A = agreeableness; C = conscientiousness; N1 – C6 = the facets; 1–20 represent items in the DDI; 1 = I feel happy; 2 = I feel sad; 3 = I feel irritable; 4 = I enjoy what I am doing; 5 = I don't care about anything; 6 = I have no appetite during the day; 7 = I worry about sleeping; 8 = I didn't have enough sleep last night; 9 = I am restless; 10 = I am tired; 11= It is not effortful to do things; 12 = I feel guilty; 13 = I am doing things at my normal pace; 14 = I feel worthless; 15 = I feel that I can't get anything done; 16 = I feel that I can't make decisions; 17 = I can't concentrate; 18 = I feel hopeless; 19 = How's your day; 20 = How would you rate your overall physical health today. There were revisions of the DDI over the course of the three studies and items 1, 12, and 16 were not included in Study 2. * $p < .05$. ** $p < .01$. *** $p < .001$.

Table 5.6 *Standardized betas of the Big Five personality traits and facets in regression models testing the relationships between personality traits and facets and the variabilities of the DDI items in Study 2*

	2	3	4	5	6	7	8	9	10
N	-.04	.06	-.09	-.05	-.14	-.15	.17	-.07	-.07
E	.07	.18	.13	.22	.13	.28	.28	.22	.35**
O	.21	.22	.14	.20	.32	.19	.21	.27	.05
A	.02	.00	.13	.14	-.01	-.05	.30	.19	.18
C	.05	-.05	.03	.06	-.08	-.19	.02	.04	.05
N1	-.05	.03	-.11	.04	-.02	-.21	.04	-.05	-.13
N2	-.05	.09	-.11	-.01	-.06	.17	.16	.04	.10
N3	.08	.10	-.07	-.05	-.17	-.14	.20	-.01	-.01
N4	-.14	-.13	.01	-.16	-.16	-.12	-.13	-.23	-.20
N5	.00	.13	.05	.10	-.11	-.24	.43**	-.04	.08
N6	.00	.08	-.18	-.11	-.06	-.06	.04	.04	-.08
E1	.04	.06	.09	.17	.02	.00	.19	.09	.30*
E2	.06	.14	.12	.23	.12	.11	.37*	.20	.36***
E3	.08	.05	.02	-.03	.03	.21	.01	.10	.10
E4	-.01	.08	.05	.15	.05	.12	.19	.03	.14
E5	.08	.33*	.10	.24	.26	.29	.18	.34*	.12
E6	.03	.02	.13	.11	.02	.38**	.14	.05	.29*
O1	.12	.14	.16	.21	.16	.31*	.18	.19	.03
O2	.20	.25	.12	.25	.42**	.28	.18	.19	.03
O3	.12	.05	.01	-.05	.15	.00	-.02	.06	-.05
O4	.18	.21	.14	.18	.20	.22	.27	.29	.19
O5	.13	.15	.12	.08	.22	.06	.08	.17	.07
O6	.01	.04	-.02	.10	.08	-.17	.02	.05	-.10
A1	.11	.02	.20	.06	-.18	.07	.23	.00	.24
A2	.07	-.03	.09	.09	.01	-.02	.16	.23	.10
A3	.11	.14	.13	.18	.15	.03	.29	.21	.15
A4	-.09	-.07	.07	.08	.06	-.16	.26	.04	.16
A5	-.11	-.10	-.01	-.01	.01	-.04	.13	.12	.01
A6	-.09	-.10	-.01	.06	.00	-.12	.10	.13	.05
C1	.05	.10	.03	.01	-.04	.02	.04	-.01	.07
C2	-.11	-.23	-.21	-.25	-.12	-.19	-.01	-.25	-.08
C3	-.11	-.24	-.06	-.17	-.06	-.22	-.05	-.06	-.10
C4	-.01	.09	.14	.00	.02	-.07	.06	.09	.05
C5	.06	-.07	-.18	-.14	-.08	-.18	-.11	-.05	-.02
C6	.14	.08	.16	.29	-.04	-.09	.04	.18	.11

	11	13	14	15	17	18	19	20
N	-.18	.15	.08	.04	.08	.03	-.22	.13
E	.33*	.23	.11	.16	.27	.24	.19	.19
O	.07	.20	.20	.09	.10	.25	.37*	.30
A	.08	.12	.08	.14	.13	.12	.24	.21
C	.00	.01	-.02	-.08	-.13	.02	.06	-.01
N1	-.32	.10	-.08	-.16	-.08	-.03	-.07	.13
N2	.05	.21	.18	.18	.26	.07	-.27	.14
N3	-.13	.16	.17	.12	.11	.08	-.12	.15
N4	-.15	-.08	-.03	-.03	-.02	-.10	-.22	-.01
N5	-.01	.18	.00	.01	.03	.05	-.18	.02
N6	-.18	.11	.12	.06	.07	.07	-.05	.15
E1	.17	.14	-.10	.06	.11	.03	.15	.03
E2	.32*	.15	.21	.18	.27	.26	.09	.26
E3	.03	.14	.11	-.03	.08	.17	.09	.08
E4	.07	.13	-.08	.02	.10	.12	.11	.07
E5	.26	.16	.25	.14	.17	.33	.11	.20
E6	.40**	.15	-.01	.23	.29	.01	.22	.08
O1	.19	.25	.12	.23	.20	.17	.15	.35*
O2	.13	.28	.19	.15	.22	.27	.26	.23
O3	-.02	.10	-.11	-.06	-.03	-.05	.34*	.09
O4	.19	.13	.23	.08	.11	.18	.27	.13
O5	.04	.13	.30	.01	.06	.25	.07	.06
O6	-.19	-.05	.00	-.01	-.11	.13	.16	.16
A1	.09	.01	-.04	.01	.04	-.05	.11	.00
A2	.08	.13	.09	.21	.17	.12	.32	.20
A3	.13	.24	.10	.20	.27	.24	.27	.15
A4	.08	.11	.04	.10	.07	-.02	.18	.14
A5	.02	.05	.13	.13	.07	.09	.11	.27
A6	-.08	-.02	-.04	-.01	-.01	.11	.09	.17
C1	.10	.10	.03	-.02	.06	.04	.04	-.04
C2	-.16	-.17	-.27	-.24	-.31	-.30	-.12	-.06
C3	-.28	-.14	-.12	-.16	-.28	-.18	.02	.01
C4	-.06	.05	.03	-.03	-.01	.07	.06	.09
C5	-.05	.05	.06	-.21	-.17	-.12	-.13	-.20
C6	.17	.11	.10	.10	.06	.20	.15	.05

Note. N = neuroticism; E = extraversion; O = openness; A = agreeableness; C = conscientiousness; N1 – C6 = the facets; 1–20 represent items in the DDI; 1 = I feel happy; 2 = I feel sad; 3 = I feel irritable; 4 = I enjoy what I am doing; 5 = I don't care about anything; 6 = I have no appetite during the day; 7 = I worry about sleeping; 8 = I didn't have enough sleep last night; 9 = I am restless; 10 = I am tired; 11= It is not effortful to do things; 12 = I feel guilty; 13 = I am doing things at my normal pace; 14 = I feel worthless; 15 = I feel that I can't get anything done; 16 = I feel that I can't make decisions; 17 = I can't concentrate; 18 = I feel hopeless; 19 = How's your day; 20 = How would you rate your overall physical health today. There were revisions of the DDI over the course of the three studies and items 1, 12, and 16 were not included in Study 2. * $p < .05$. ** $p < .01$. *** $p < .001$.

Study 3

H12 and H13 were supported. MD severity was positively predicted by neuroticism and negative predicted by extraversion and conscientiousness (Table 5.7). The facets depression under neuroticism and cheerfulness under extraversion significantly predicted MD severity, too. There were other facets that significantly predicted MD severity including N1 anxiety, N5 immoderation, N6 vulnerability, E1 friendliness, C1 self-efficacy, C2 orderliness, C4 achievement-striving, C5 self-discipline, and C6 cautiousness. A facet under agreeableness - A1 trust - significantly predicted MD severity. Several facets significantly predicted some PHQ-9 items. Among these facets, N1 anxiety, N3 depression, N5 immoderation, N6 vulnerability, E6 cheerfulness, C1 self-efficacy, C2 orderliness, C4 achievement-striving, and C5 self-discipline were significant predictors of more than five PHQ-9 items.

The mean momentary ratings of some items in the DDI were significantly predicted by high neuroticism, low extraversion, and low conscientiousness (Table 5.8). All facets under neuroticism, extraversion, and conscientiousness significantly predicted the momentary ratings of some DDI items except N4 self-consciousness and E5 excitement-seeking. There were several facets under openness and agreeableness significantly predicted the momentary ratings of some DDI items. The variability of a few DDI items were significantly predicted by personality traits and facets (Table 5.9).

High neuroticism was the only consistent personality trait that significantly predicted MD severity in the three studies. The results in Studies 1 and 3 suggested low extraversion and low conscientiousness significantly predicted MD severity but this was not supported by the results in Study 2. Consistent with Studies 1 and 2, significant associations were only observed between personality traits and facets and some items in the PHQ-9 and the DDI, thus supporting heterogeneity in MD symptoms.

To further test the robustness of the results, replicability of the results and meta-analyses were conducted.

Table 5.7 *Standardized betas of the Big Five personality traits and facets in regression models testing the relationships between personality traits and facets and the PHQ-9 items in Study 3*

	PHQ-9	1	2	3	4	5	6	7	8	9
N	.58***	.58***	.50***	.33*	.55***	.39***	.51***	.34*	.30	.37**
E	-.38***	-.45***	-.31*	-.24	-.27	-.20	-.44***	-.28*	-.13	-.16
O	-.01	-.11	.04	.04	-.05	-.03	-.03	.00	.01	.08
A	-.24	-.25	-.18	-.15	-.28	-.23	-.09	-.14	-.18	-.13
C	-.50***	-.40***	-.45***	-.25	-.41***	-.31*	-.43***	-.47***	-.29*	-.41***
N1	.46***	.37**	.38**	.28	.43***	.32*	.43***	.28*	.23	.35*
N2	.11	.27	.18	.00	.20	.00	.08	-.01	.03	-.01
N3	.65***	.55***	.60***	.41***	.55***	.38***	.64***	.40***	.36**	.50***
N4	.16	.28	.08	.10	.14	.14	.17	.11	.03	-.01
N5	.44***	.37**	.34*	.31*	.46***	.44***	.28	.24	.25	.23
N6	.55***	.56***	.50***	.26	.47***	.33*	.47***	.37**	.32*	.46***
E1	-.34*	-.38***	-.21	-.17	-.28	-.26	-.30*	-.30*	-.17	-.16
E2	-.19	-.30*	-.16	-.05	-.09	-.13	-.24	-.19	-.05	-.08
E3	-.17	-.21	-.17	-.17	-.09	-.09	-.24	-.16	.00	.02
E4	-.24	-.26	-.18	-.13	-.17	-.12	-.35**	-.12	-.13	-.16
E5	-.06	-.17	-.06	-.08	-.04	.02	-.17	-.01	.09	.11
E6	-.55***	-.55***	-.50***	-.41***	-.45***	-.24	-.51***	-.36**	-.25	-.39***
O1	.04	.09	.05	.05	.02	-.01	-.03	.03	-.04	.09
O2	-.06	-.16	.00	-.07	-.14	.01	.03	-.06	-.08	.04
O3	.08	-.02	.09	.12	.09	.06	-.06	.08	.15	.04
O4	-.07	-.17	-.09	.04	-.09	-.06	-.09	-.01	.06	-.01
O5	-.18	-.13	-.14	-.11	-.20	-.13	-.16	-.17	-.16	.00
O6	.15	-.02	.26	.08	.10	.00	.21	.13	.11	.14
A1	-.39***	-.36*	-.25	-.29	-.38**	-.26	-.29	-.29	-.28	-.26
A2	-.27	-.22	-.25	-.22	-.27	-.12	-.20	-.17	-.19	-.24
A3	-.22	-.25	-.20	-.04	-.20	-.15	-.18	-.19	-.10	-.16
A4	.00	.01	.06	-.06	-.08	-.05	.10	.05	-.04	.03
A5	.20	.18	.20	.11	.15	-.01	.32*	.12	.08	.22
A6	-.24	-.32*	-.27	-.08	-.30*	-.31*	-.07	-.04	-.16	-.09
C1	-.37**	-.31*	-.34*	-.18	-.21	-.02	-.37**	-.39***	-.33*	-.41***
C2	-.44***	-.29	-.34*	-.39***	-.44***	-.37***	-.36**	-.38***	-.06	-.18
C3	-.16	-.14	-.13	-.02	-.18	-.15	-.13	-.18	-.03	-.13
C4	-.36***	-.34*	-.30*	-.09	-.24	-.22	-.34*	-.35**	-.30*	-.36**
C5	-.42***	-.38**	-.41***	-.16	-.27	-.24	-.43***	-.42***	-.25	-.29*
C6	-.31*	-.22	-.30*	-.13	-.29	-.20	-.19	-.23	-.23	-.34*

Note. PHQ-9 = PHQ-9 total score; 1–9 = items in the PHQ-9; N = neuroticism; E = extraversion; O = openness; A = agreeableness; C = conscientiousness; N1 – C6 = the facets. * $p < .05$. ** $p < .01$. *** $p < .001$.

Table 5.8 *Standardized betas of the Big Five personality traits and facets in regression models testing the relationships between personality traits and facets and the mean momentary ratings of the DDI items in Study 3*

	1	2	3	4	5	6	7	8	9
N	.46***	.43***	.31	.50***	.38**	.17	-.11	.19	.33*
E	-.36**	-.29*	-.21	-.28	-.45***	-.12	.07	-.06	-.20
O	.07	.12	-.08	-.05	-.08	-.01	-.18	.07	-.08
A	-.17	-.23	-.27	-.21	-.35**	-.22	.00	-.04	-.20
C	-.48***	-.44***	-.33*	-.45***	-.46***	-.18	.05	-.24	-.25
N1	.30*	.33*	.18	.35*	.12	.03	-.01	.07	.28
N2	.22	.09	.35*	.28	.15	.21	.06	-.01	.20
N3	.56***	.58***	.26	.54***	.40***	.29*	-.13	.24	.36**
N4	.18	.12	.12	.17	.27	-.03	.00	.07	.10
N5	.20	.23	.09	.25	.25	.12	-.25	.23	.12
N6	.43***	.39**	.28	.46***	.37**	.08	-.10	.16	.31*
E1	-.35*	-.34**	-.28	-.30*	-.44***	-.13	.01	-.03	-.28
E2	-.27	-.24	-.22	-.16	-.33*	-.07	-.14	.05	-.15
E3	-.13	-.10	-.11	-.16	-.29*	.09	.17	-.19	-.03
E4	-.20	-.11	.01	-.05	-.31*	-.05	.05	-.08	-.02
E5	.09	.16	.09	.12	.01	.04	.00	.16	.00
E6	-.60***	-.53***	-.32*	-.55***	-.44***	-.37**	.19	-.14	-.32*
O1	.12	.17	.05	.00	.16	-.07	-.15	.15	.00
O2	.01	.03	-.16	-.09	-.20	-.07	-.05	-.01	-.11
O3	-.04	-.01	.06	-.03	-.13	-.05	-.06	.08	-.08
O4	-.02	.02	-.19	-.07	-.14	-.01	-.16	-.05	-.07
O5	-.05	-.07	-.17	-.15	-.07	.07	-.04	-.16	-.14
O6	.24	.31*	.12	.18	.12	.14	-.21	.22	.11
A1	-.28	-.33*	-.27	-.37*	-.37**	-.22	-.05	-.04	-.40**
A2	-.15	-.23	-.15	-.18	-.32*	-.17	.12	-.11	-.11
A3	-.18	-.22	-.17	-.17	-.34*	-.16	.05	-.08	-.10
A4	.03	-.03	-.16	-.01	-.10	-.15	-.02	.13	-.07
A5	.13	.08	-.13	.15	.10	-.02	-.07	.11	.04
A6	-.19	-.17	-.20	-.20	-.34**	-.14	-.02	-.16	-.13
C1	-.35*	-.29*	-.04	-.35*	-.32*	-.14	.13	-.24	-.02
C2	-.32*	-.27	-.39***	-.31*	-.41***	-.13	.03	-.11	-.30*
C3	-.29	-.27	-.27	-.16	-.32*	-.08	.12	-.03	-.05
C4	-.32*	-.29*	-.20	-.31*	-.41***	-.13	-.06	-.14	-.10
C5	-.35*	-.28	-.19	-.32*	-.37**	-.09	.06	-.09	-.15
C6	-.36**	-.41***	-.24	-.41***	-.11	-.18	.01	-.31*	-.28

	10	12	13	14	16	17	18	19	20
N	.31*	.50***	.28	.52***	.56***	.55***	.54***	.49***	.30*
E	-.23	-.49***	-.29	-.41***	-.45***	-.43***	-.40***	-.38***	-.10
O	.02	-.15	.00	-.05	-.13	-.14	-.07	-.02	.09
A	-.08	-.14	-.11	-.21	-.20	-.30*	-.21	-.19	-.09
C	-.20	-.37**	-.14	-.48***	-.54***	-.60***	-.49***	-.42***	-.35**
N1	.22	.26	.19	.29	.31*	.34*	.35**	.30*	.22
N2	.18	.18	.18	.15	.20	.24	.16	.27	.11
N3	.38**	.56***	.28	.67***	.63***	.59***	.67***	.53***	.33*
N4	.18	.27	.23	.18	.24	.24	.16	.24	.05
N5	.12	.31*	.05	.30*	.40***	.34*	.35*	.26	.25
N6	.17	.43***	.23	.50***	.50***	.51***	.51***	.39**	.27
E1	-.27	-.46***	-.18	-.42***	-.41***	-.45***	-.40***	-.35**	.00
E2	-.11	-.30*	-.29	-.25	-.30*	-.32*	-.26	-.20	.00
E3	-.19	-.29*	-.05	-.28	-.31*	-.27	-.20	-.19	.06
E4	.01	-.25	-.15	-.17	-.18	-.15	-.16	-.19	-.25
E5	.01	-.16	-.22	.03	-.04	.04	.00	-.03	.05
E6	-.37**	-.56***	-.31*	-.58***	-.57***	-.57***	-.59***	-.60***	-.29*
O1	.19	-.01	-.03	.04	-.02	.05	-.03	.05	-.05
O2	-.03	-.11	-.01	-.06	-.07	-.08	-.06	-.04	.02
O3	-.01	-.17	.05	-.12	-.04	-.05	-.09	-.09	.15
O4	-.15	-.13	-.08	-.08	-.16	-.17	-.09	-.01	.17
O5	-.11	-.28	-.07	-.19	-.32*	-.36**	-.20	-.11	-.06
O6	.20	.15	.14	.23	.11	.09	.22	.15	.10
A1	-.19	-.25	-.01	-.32*	-.34*	-.39**	-.36*	-.25	-.12
A2	-.03	-.12	-.03	-.20	-.18	-.30*	-.19	-.14	-.15
A3	-.15	-.29*	-.11	-.32*	-.30*	-.33*	-.27	-.21	.05
A4	.04	.12	.05	.05	.05	-.04	.04	-.02	-.01
A5	.16	.23	-.17	.25	.28	.18	.25	.11	.04
A6	-.13	-.24	-.18	-.27	-.27	-.30*	-.27	-.24	-.13
C1	-.17	-.29*	-.08	-.42***	-.52***	-.52***	-.40***	-.33*	-.27
C2	-.11	-.37**	-.09	-.34*	-.31*	-.39***	-.37**	-.29	-.17
C3	-.04	-.15	.11	-.15	-.15	-.26	-.16	-.25	-.12
C4	-.13	-.22	-.21	-.37**	-.44***	-.49***	-.35**	-.27	-.19
C5	-.14	-.41***	-.22	-.36**	-.52***	-.54***	-.40***	-.36**	-.36**
C6	-.20	-.10	-.03	-.33*	-.28	-.30*	-.32*	-.27	-.32*

Note. N = neuroticism; E = extraversion; O = openness; A = agreeableness; C = conscientiousness; N1 – C6 = the facets; 1–20 represent items in the DDI; 1 = I feel happy; 2 = I feel sad; 3 = I feel irritable; 4 = I enjoy what I am doing; 5 = I don't care about anything; 6 = I have no appetite during the day; 7 = I worry about sleeping; 8 = I didn't have enough sleep last night; 9 = I am restless; 10 = I am tired; 11= It is not effortful to do things; 12 = I feel guilty; 13 = I am doing things at my normal pace; 14 = I feel worthless; 15 = I feel that I can't get anything done; 16 = I feel that I can't make decisions; 17 = I can't concentrate; 18 = I feel hopeless; 19 = How's your day; 20 = How would you rate your overall physical health today. There were revisions of the DDI over the course of the three studies and items 11 and 15 were not included in Study 3. * $p < .05$. ** $p < .01$. *** $p < .001$.

Table 5.9 *Standardized betas of the Big Five personality traits and facets in regression models testing the relationships between personality traits and facets and the variabilities of the DDI items in Study 3*

	1	2	3	4	5	6	7	8	9	10
N	.10	.07	.27	.20	.25	-.02	-.09	.05	.12	.00
E	.03	.07	-.02	.06	-.09	.16	.05	.06	.01	.09
O	.08	.19	-.02	.06	.11	.09	.35**	.08	.12	.09
A	.18	.12	.04	.09	-.14	.03	.11	.09	.01	.08
C	-.01	.01	-.09*	-.02*	-.25	.01	.10	.05	.01	.09
N1	.29	.21	.31	.27	.18	.09	-.08	.08	.21	.13
N2	.00	.06	.18	.12	.08	-.11	-.04	-.02	.04	-.07
N3	.05	.09	.11	.04	.18	.03	-.04	-.07	-.01	-.12
N4	.00	-.01	.17	.06	.13	-.11	-.04	.06	.04	.00
N5	.03	-.11	.17	.21	.16	.07	-.10	.18	.14	-.01
N6	.05	.03	.18	.12	.30*	-.07	-.08	-.03	.09	.05
E1	.06	-.03	-.07	.04	-.18	.13	.08	.11	-.07	.09
E2	-.01	-.08	-.08	.00	-.16	.05	.09	.13	-.02	.03
E3	.19	.31*	.12	.10	.14	.31*	.03	.01	.15	.14
E4	-.02	.08	.05	.15	-.14	.12	.01	-.13	.01	-.06
E5	-.08	.12	.01	-.07	.18	.07	.07	-.11	.03	.11
E6	-.02	-.09	-.08	.01	-.17	-.02	-.11	.21	-.06	.06
O1	.14	.19	.08	.06	.24	-.05	.26	.16	.25	.22
O2	.20	.25	.01	.14	.09	.16	.19	.16	.14	.17
O3	-.10	-.05	-.07	-.02	-.13	.06	.06	.10	-.20	-.09
O4	-.07	.01	-.10	-.04	-.04	.05	.18	-.05	.06	.03
O5	.13	.20	.04	.08	.22	.18	.30*	.01	.19	.12
O6	-.02	.08	-.03	-.02	.04	-.06	.30*	-.12	-.02	-.15
A1	.19	.00	.09	.06	-.11	-.08	.25	.06	.02	.23
A2	.15	.16	.06	.04	-.25	.06	-.05	.16	-.03	.11
A3	.17	.19	.03	.12	-.10	.09	.11	.11	.01	-.02
A4	.13	.08	.05	.09	.01	.00	.04	.02	.02	-.01
A5	.03	.03	-.04	.01	.07	-.05	-.04	-.06	-.07	-.08
A6	.04	.05	-.04	.06	-.16	.11	.11	.08	.08	.03
C1	.04	.04	.02	.02	-.12	.00	.07	.12	.15	.10
C2	.05	.08	-.04	-.02	-.14	.06	.10	.08	.04	.21
C3	.02	-.03	.14	.17	-.17	.02	-.12	-.08	.11	.13
C4	-.06	.04	-.19	-.09	-.28*	-.01	.15	.02	-.10	-.03
C5	-.05	.09	-.12	-.04	-.16	-.03	.12	.01	-.05	.08
C6	-.06	-.19	-.10	-.06	-.17	-.04	-.02	.01	-.08	-.10

	12	13	14	16	17	18	19	20
N	.15	.05	.11	.20	.12	.00	.01	-.07
E	.06	.04	.07	-.01	.00	.18	.11	.09
O	.12	.01	.19	.19	.05	.22	.03	-.01
A	.01	.01	.02	.14	-.03	.11	.02	-.01
C	.10	.03	.01	-.10	.03	.07	.11	.25
N1	.19	.14	.16	.13	.16	.15	.18	-.05
N2	.08	-.09	-.01	.04	.06	-.06	.01	.08
N3	.08	.10	.15	.17	-.02	-.01	-.05	-.21
N4	-.03	-.04	-.07	.11	.19	-.15	-.06	-.03
N5	.22	.00	.13	.21	.02	.08	.02	-.01
N6	.07	.08	.10	.18	.10	-.01	-.05	-.04
E1	.06	.04	.08	-.05	-.17	.14	.09	.11
E2	.06	-.06	-.05	-.05	-.12	.06	.02	.18
E3	.24	.18	.20	.03	.17	.27*	.26	.13
E4	.01	.06	.09	.10	.12	.16	.07	-.02
E5	-.07	.00	.06	.10	.09	.11	-.04	-.16
E6	-.11	-.06	-.11	-.14	-.05	.00	.03	.07
O1	.11	-.08	.12	.13	.20	.10	.00	-.06
O2	.14	.09	.22	.20	.10	.23	.13	-.08
O3	-.06	-.05	-.09	.00	-.12	-.04	-.11	.03
O4	.07	.01	.08	.07	-.10	.05	-.05	-.03
O5	.13	.04	.21	.17	.11	.29*	.19	.10
O6	.04	.05	.17	.13	.00	.21	-.02	.03
A1	.04	.01	-.08	.08	-.03	.11	-.04	.16
A2	-.02	-.01	-.04	.03	.05	.02	.10	-.08
A3	.08	-.02	.05	.06	-.08	.17	.08	.05
A4	.07	.09	.15	.15	.00	.17	.01	-.01
A5	-.08	-.12	.06	.16	-.09	-.10	-.11	-.15
A6	-.04*	.09	-.04	.08	.03	.09	.03	-.01
C1	.29	-.08	.03	-.14	.14	.21	.21	.25
C2	-.07	.19	-.01	.07	.09	-.02	.11	.17
C3	.02	.10	.11	.06	.04	.03	.10	.11
C4	.18	-.09	.06	-.09	-.06	.08	.07	.19
C5	.10	-.04	.07	-.13	.01	.13	.11	.13
C6	-.05	.00	-.14	-.17	-.07	-.09	-.11	.20

Note. N = neuroticism; E = extraversion; O = openness; A = agreeableness; C = conscientiousness; N1 – C6 = the facets; 1–20 represent items in the DDI; 1 = I feel happy; 2 = I feel sad; 3 = I feel irritable; 4 = I enjoy what I am doing; 5 = I don't care about anything; 6 = I have no appetite during the day; 7 = I worry about sleeping; 8 = I didn't have enough sleep last night; 9 = I am restless; 10 = I am tired; 11= It is not effortful to do things; 12 = I feel guilty; 13 = I am doing things at my normal pace; 14 = I feel worthless; 15 = I feel that I can't get anything done; 16 = I feel that I can't make decisions; 17 = I can't concentrate; 18 = I feel hopeless; 19 = How's your day; 20 = How would you rate your overall physical health today. There were revisions of the DDI over the course of the three studies and items 11 and 15 were not included in Study 3. * $p < .05$. ** $p < .01$. *** $p < .001$.

Replicability across Studies 1, 2 and 3

Replicability was tested by correlating standardized betas extracted from regression models in the three studies. The association between extraversion and PHQ-9 score replicated nicely across the three studies as seen in the correlations ranged from medium to high. The correlation coefficients of the mean momentary DDI ratings and three personality traits – extraversion, agreeableness, and conscientiousness were medium to high so these associations replicated across the three studies, too (Table 5.10). The correlations between neuroticism and the PHQ-9 score, the mean momentary ratings, and the variability of momentary ratings were all positive but some correlations were small while others were large. Therefore, they might not reproduce well. The other comparisons were rather inconsistent with both negative and positive correlations.

Table 5.10 *Spearman's rhos of the standardized betas of personality traits and PHQ-9 score, mean momentary ratings, and standard deviations of momentary ratings from regression models in Studies 1, 2, and 3*

		r		
		Study 1 vs. Study 2	Study 1 vs. Study 3	Study 2 vs. Study 3
PHQ-9 score	N	.74	.18	.53
	E	.93	.58	.43
	O	.24	.39	.07
	A	.53	-.53	-.29
	C	.20	.42	.11
Mean momentary DDI ratings	N	.26	.78	.24
	E	.31	.54	.53
	O	.12	-.24	-.10
	A	.49	.26	.55
	C	.73	.52	.34
SD of momentary DDI ratings	N	.23	.15	.17
	E	.70	-.37	-.14
	O	-.10	-.24	-.16
	A	.10	.27	-.37
	C	.05	.56	-.08

Note. *r* = Spearman's rho; *p* = *p*-value; N = neuroticism; E = extraversion; O = openness; A = agreeableness; C = conscientiousness.

Meta-analysis

The results from the three studies either partially (Study 2) or fully (Studies 1 and 3) supported the hypotheses (H12 and H13). Meta-analysis of the three studies was conducted to test the existence of common effects across the three studies. Sample size of each study and standardized betas and standard errors of the personality traits and facets from the regression models were used in the meta-analysis.

Meta-analysis found that in all or most of the items in the PHQ-9, high neuroticism, low extraversion, and low conscientiousness influenced MD severity as indicated by increasing PHQ-9 scores. The effects were asymmetrical across items with ranges of .32–.58, -.15–-.41, and -.19–-.37, for neuroticism, extraversion, and conscientiousness, respectively. The spreading out of the betas in neuroticism (.26) and extraversion (.28) may indicate MD symptom heterogeneity.

For neuroticism and conscientiousness, the *p*-values of all PHQ-9 items were smaller than .01. As for extraversion, two items had a *p*-value greater than .05. These may indicate some level of MD symptom homogeneity because all or most of the PHQ-9 items had a significant alpha level. Openness and agreeableness had inconsistent and small effects on the PHQ-9 items because the betas were very close to zero and there were negative and positive values. Tables 5.11–5.15 show the meta-analysis results across the three studies for the PHQ-9 items and neuroticism, extraversion, openness, agreeableness, and conscientiousness, respectively.

Table 5.11 *Meta-analysis of neuroticism and the PHQ-9 items across the three studies* (*N* = 277)

PHQ-9 item	*β*	*SE*	*z*	*p*
Little interest or pleasure in doing things	.52	.06	9.22	< .001
Feeling down, depressed, or hopeless	.53	.06	9.54	<.001
Trouble falling or staying asleep, or sleeping too much	.46	.06	8.13	< .001
Feeling tired or having little energy	.50	.06	9.07	< .001
Poor appetite or overeating	.35	.06	5.97	< .001
Feeling bad about yourself	.58	.05	10.68	< .001
Trouble concentrating on things	.40	.06	6.91	< .001
Psychomotor changes	.32	.06	5.26	< .001
Suicidal ideation	.40	.06	6.49	< .001

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.12 *Meta-analysis of extraversion and the PHQ-9 items across the three studies* (*N* = 277)

PHQ-9 item	*β*	*SE*	*z*	*p*
Little interest or pleasure in doing things	-.37	.06	-6.65	< .001
Feeling down, depressed, or hopeless	-.36	.06	-6.31	< .001
Trouble falling or staying asleep, or sleeping too much	-.22	.06	-3.55	< .001
Feeling tired or having little energy	-.20	.06	-3.34	.008
Poor appetite or overeating	-.15	.06	-2.48	.064
Feeling bad about yourself	-.41	.06	-7.37	< .001
Trouble concentrating on things	-.19	.06	-3.11	.014
Psychomotor changes	-.15	.06	-2.37	.081
Suicidal ideation	-.29	.06	-4.72	< .001

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.13 *Meta-analysis of openness and the PHQ-9 items across the three studies* (*N* = 277)

PHQ-9 item	*β*	*SE*	*z*	*p*
Little interest or pleasure in doing things	-.03	.06	-.53	.796
Feeling down, depressed, or hopeless	.03	.06	.55	.785
Trouble falling or staying asleep, or sleeping too much	.04	.07	.62	.754
Feeling tired or having little energy	.02	.06	.33	.879
Poor appetite or overeating	.05	.06	.75	.693
Feeling bad about yourself	-.04	.07	-.55	.785
Trouble concentrating on things	.10	.06	1.54	.317
Psychomotor changes	.06	.07	.98	.579
Suicidal ideation	.07	.07	1.10	.515

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.14 *Meta-analysis of agreeableness and the PHQ-9 items across the three studies* (*N* = 277)

PHQ-9 item	*β*	*SE*	*z*	*p*
Little interest or pleasure in doing things	-.02	.06	-.35	.871
Feeling down, depressed, or hopeless	.00	.06	.00	1.000
Trouble falling or staying asleep, or sleeping too much	-.02	.06	-.37	.863
Feeling tired or having little energy	.06	.06	1.08	.529
Poor appetite or overeating	-.06	.06	-.94	.596
Feeling bad about yourself	-.01	.06	-.17	.948
Trouble concentrating on things	-.01	.06	-.09	.973
Psychomotor changes	-.07	.06	-1.18	.475
Suicidal ideation	-.01	.06	-.20	.932

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.15 *Meta-analysis of conscientiousness and the PHQ-9 items across the three studies* (*N* = 277)

PHQ-9 item	*β*	*SE*	*z*	*p*
Little interest or pleasure in doing things	-.28	.06	-4.63	< .001
Feeling down, depressed, or hopeless	-.26	.06	-4.45	< .001
Trouble falling or staying asleep, or sleeping too much	-.22	.06	-3.35	.008
Feeling tired or having little energy	-.25	.06	-4.12	< .001
Poor appetite or overeating	-.19	.06	-3.23	.008
Feeling bad about yourself	-.37	.06	-6.16	< .001
Trouble concentrating on things	-.35	.06	-5.90	< .001
Psychomotor changes	-.21	.06	-3.42	.008
Suicidal ideation	-.23	.06	-3.66	< .001

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Similar results were observed in the mean momentary ratings of the DDI items – high neuroticism, low extraversion, and low conscientiousness predicted higher mean momentary ratings. The ranges of the standardized betas for neuroticism, extraversion, and conscientiousness and the mean momentary ratings of the DDI items were .14–.56, -.03–-.49, and -.06–-.54, respectively. These revealed a considerable amount of between-item variances. While the mean momentary ratings of nearly all DDI items were significantly predicted by neuroticism, extraversion, and conscientiousness may imply MD symptom homogeneity. The ranges of the betas showed the differences between MD symptoms and may indicate certain level of heterogeneity in MD symptoms. Most of the *p*-values were

smaller than .05. Doing things with one's normal pace was the only item with an insignificant alpha in neuroticism. This item was neither significant in extraversion nor conscientiousness. Similar to the meta-analysis results of the PHQ-9 items as described previously, openness and agreeableness had asymmetrical effects on the mean ratings of the DDI items and almost all *p*-values were insignificant except one DDI item in agreeableness. The meta-analysis results of the mean momentary ratings of each DDI item and the Big Five personality traits were listed in Tables 5.16–5.20.

Table 5.16 *Meta-analysis of neuroticism and the mean momentary ratings of the DDI items across the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	.46	.11	4.18	< .001
I feel sad.	.46	.06	8.23	< .001
I feel irritable.	.42	.06	7.45	< .001
I enjoy what I am doing.	.46	.06	8.23	< .001
I don't care about anything.	.33	.06	5.68	< .001
I have no appetite during the day.	.22	.06	3.55	< .001
I worry about sleeping.	.28	.06	4.71	< .001
I didn't have enough sleep last night.	.36	.06	6.13	< .001
I am restless.	.34	.06	5.52	< .001
I am tired.	.43	.06	7.50	< .001
It is not effortful to do things.	.28	.07	3.93	< .001
I feel guilty.	.50	.10	5.00	< .001
I am doing things at my normal pace.	.14	.09	1.54	.319
I feel worthless.	.51	.05	10.08	< .001
I feel that I can't get anything done.	.56	.06	9.43	< .001
I feel that I can't make decisions.	.56	.10	5.60	< .001
I can't concentrate.	.55	.05	10.81	< .001
I feel hopeless.	.53	.05	10.31	< .001
How's your day?	.41	.06	7.40	< .001
How would you rate your overall physical health today?	.28	.08	3.32	.008

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.17 *Meta-analysis of extraversion and the mean momentary ratings of the DDI items across the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	-.36	.11	-3.27	.008
I feel sad.	-.40	.06	-7.20	< .001
I feel irritable.	-.32	.06	-5.76	< .001
I enjoy what I am doing.	-.33	.06	-5.83	< .001
I don't care about anything.	-.38	.05	-7.09	< .001
I have no appetite during the day.	-.12	.06	-1.94	.181
I worry about sleeping.	-.16	.06	-2.49	.064
I didn't have enough sleep last night.	-.14	.06	-2.15	.123
I am restless.	-.18	.06	-2.90	.025
I am tired.	-.22	.06	-3.82	< .001
It is not effortful to do things.	-.16	.07	-2.42	.074
I feel guilty.	-.49	.09	-5.44	< .001
I am doing things at my normal pace.	-.03	.08	-.32	.883
I feel worthless.	-.38	.05	-6.96	< .001
I feel that I can't get anything done.	-.36	.07	-5.36	< .001
I feel that I can't make decisions.	-.45	.10	-4.50	< .001
I can't concentrate.	-.34	.06	-6.06	< .001
I feel hopeless.	-.38	.06	-6.80	< .001
How's your day?	-.37	.06	-6.65	< .001
How would you rate your overall physical health today?	-.11	.08	-1.29	.424

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.18 *Meta-analysis of openness and the mean momentary ratings of the DDI items across the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	.00	.11	.00	1.000
I feel sad.	.04	.06	.59	.770
I feel irritable.	-.01	.06	-.10	.971
I enjoy what I am doing.	.02	.06	.40	.850
I don't care about anything.	-.10	.06	-1.70	.258
I have no appetite during the day.	.12	.06	1.87	.202
I worry about sleeping.	.01	.06	.15	.955
I didn't have enough sleep last night.	.07	.06	1.17	.477
I am restless.	.14	.06	2.26	.102
I am tired.	.02	.06	.25	.911
It is not effortful to do things.	-.06	.07	-.82	.658
I feel guilty.	.00	.11	.00	1.000
I am doing things at my normal pace.	.00	.09	.00	1.000
I feel worthless.	.04	.06	.66	.734
I feel that I can't get anything done.	-.05	.07	-.64	.745
I feel that I can't make decisions.	.00	.11	.00	1.000
I can't concentrate.	-.03	.06	-.46	.824
I feel hopeless.	.07	.06	1.17	.480
How's your day?	.08	.06	1.27	.433
How would you rate your overall physical health today?	.03	.09	.40	.851

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.19 *Meta-analysis of agreeableness and the mean momentary ratings of the DDI items across the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	-.17	.11	-1.55	.316
I feel sad.	-.16	.06	-2.55	.056
I feel irritable.	-.11	.06	-1.87	.199
I enjoy what I am doing.	-.11	.06	-1.84	.210
I don't care about anything.	-.21	.06	-3.67	< .001
I have no appetite during the day.	-.12	.06	-1.99	.164
I worry about sleeping.	-.04	.06	-.60	.763
I didn't have enough sleep last night.	.04	.06	.57	.778
I am restless.	-.09	.06	-1.52	.325
I am tired.	.04	.06	.77	.682
It is not effortful to do things.	.00	.07	-.05	.980
I feel guilty.	-.14	.11	-1.27	.431
I am doing things at my normal pace.	-.01	.09	-.14	.959
I feel worthless.	-.09	.06	-1.46	.348
I feel that I can't get anything done.	.01	.07	.09	.972
I feel that I can't make decisions.	-.20	.11	-1.82	.217
I can't concentrate.	-.09	.06	-1.46	.348
I feel hopeless.	-.09	.06	-1.52	.322
How's your day?	-.13	.06	-2.10	.134
How would you rate your overall physical health today?	-.06	.08	-.67	.727

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.20 *Meta-analysis of conscientiousness and the mean momentary ratings of the DDI items across the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	-.48	.10	-4.80	< .001
I feel sad.	-.29	.06	-5.01	< .001
I feel irritable.	-.28	.06	-4.83	< .001
I enjoy what I am doing.	-.29	.06	-4.99	< .001
I don't care about anything.	-.31	.06	-5.51	< .001
I have no appetite during the day.	-.16	.06	-2.50	.060
I worry about sleeping.	-.13	.06	-2.16	.123
I didn't have enough sleep last night.	-.26	.06	-4.30	< .001
I am restless.	-.21	.06	-3.41	.008
I am tired.	-.24	.06	-4.11	< .001
It is not effortful to do things.	-.09	.07	-1.23	.454
I feel guilty.	-.37	.10	-3.70	< .001
I am doing things at my normal pace.	-.06	.09	-.70	.716
I feel worthless.	-.33	.06	-5.80	< .001
I feel that I can't get anything done.	-.36	.07	-5.35	< .001
I feel that I can't make decisions.	-.54	.09	-6.00	< .001
I can't concentrate.	-.41	.05	-7.72	< .001
I feel hopeless.	-.33	.06	-5.67	< .001
How's your day?	-.28	.06	-4.78	< .001
How would you rate your overall physical health today?	-.30	.08	-3.97	< .001

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

The meta-analysis of the variabilities in the DDI items yielded slightly different results compared to the meta-analysis results of the PHQ-9 items and the mean momentary ratings of the DDI items. Most of the standardized betas had insignificant *p*-values – significant results for neuroticism, extraversion, and conscientiousness were found in 10, two, and two DDI items, respectively. Even though most items were affected by high neuroticism and low conscientiousness, the betas were relatively uneven with both negative and positive values. The effect of extraversion was relatively low in most of the DDI items. High openness and high agreeableness both contributed to a varied symptom profile.

Heterogeneity in MD symptoms could be observed in the sporadic significance found in the links between personality traits and the PHQ-9 and the DDI items. In addition, the coverages of the betas were substantially broad, indicating

MD symptom heterogeneity, too (neuroticism: -.03–.30; extraversion: -.02–.21; conscientiousness: -.19–.13). The meta-analysis results were shown in Tables 5.21–5.25. Figures 5.1–5.5, 5.6–5.10, and 5.11–5.15 are the standardized betas of the Big Five personality traits and three sets of MD measures – the PHQ-9 items, the mean momentary ratings of the DDI items, and the standard deviations of the momentary ratings of the DDI items from the three studies and meta-analyses, respectively.

Table 5.21 *Meta-analysis of neuroticism and the variabilities of the DDI items across the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	.10	.12	.83	.653
I feel sad.	.21	.06	3.33	.008
I feel irritable.	.22	.06	3.63	< .001
I enjoy what I am doing.	.21	.06	3.45	.008
I don't care about anything.	.30	.06	5.10	< .001
I have no appetite during the day.	.17	.06	2.66	.044
I worry about sleeping.	.04	.06	.71	.711
I didn't have enough sleep last night.	.13	.07	2.02	.156
I am restless.	.19	.06	3.03	.014
I am tired.	-.02	.06	-.36	.867
It is not effortful to do things.	-.03	.08	-.37	.864
I feel guilty.	.15	.12	1.25	.441
I am doing things at my normal pace.	.09	.08	1.09	.521
I feel worthless.	.30	.06	5.08	< .001
I feel that I can't get anything done.	.23	.07	3.22	.008
I feel that I can't make decisions.	.20	.10	2.00	.164
I can't concentrate.	.26	.06	4.47	< .001
I feel hopeless.	.26	.06	4.54	< .001
How's your day?	.10	.06	1.73	.247
How would you rate your overall physical health today?	.02	.08	.26	.908

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.22 *Meta-analysis of extraversion and the variabilities of the DDI items across the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	.03	.11	.27	.904
I feel sad.	-.01	.06	-.16	.950
I feel irritable.	.04	.06	.73	.704
I enjoy what I am doing.	.00	.06	-.06	.979
I don't care about anything.	-.02	.06	-.34	.877
I have no appetite during the day.	-.01	.06	-.15	.956
I worry about sleeping.	.11	.06	1.82	.215
I didn't have enough sleep last night.	.09	.06	1.46	.347
I am restless.	.03	.06	.52	.799
I am tired.	.21	.06	3.63	< .001
It is not effortful to do things.	.19	.07	2.63	.048
I feel guilty.	.06	.11	.55	.788
I am doing things at my normal pace.	.12	.08	1.42	.364
I feel worthless.	-.02	.06	-.31	.890
I feel that I can't get anything done.	.04	.07	.53	.794
I feel that I can't make decisions.	-.01	.10	-.10	.970
I can't concentrate.	.02	.06	.39	.857
I feel hopeless.	.05	.06	.89	.623
How's your day?	.05	.06	.90	.620
How would you rate your overall physical health today?	.14	.08	1.67	.269

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.23 *Meta-analysis of openness and the variabilities of the DDI items across the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	.08	.11	.73	.704
I feel sad.	.17	.06	2.79	.031
I feel irritable.	.13	.06	2.06	.145
I enjoy what I am doing.	.09	.06	1.58	.300
I don't care about anything.	.11	.06	1.82	.217
I have no appetite during the day.	.09	.06	1.37	.385
I worry about sleeping.	.18	.06	2.88	.025
I didn't have enough sleep last night.	.14	.06	2.15	.125
I am restless.	.13	.06	2.12	.131
I am tired.	.10	.06	1.67	.271
It is not effortful to do things.	.08	.08	1.04	.547
I feel guilty.	.12	.11	1.09	.521
I am doing things at my normal pace.	.08	.09	.95	.589
I feel worthless.	.15	.06	2.39	.078
I feel that I can't get anything done.	.17	.07	2.41	.074
I feel that I can't make decisions.	.19	.10	1.90	.191
I can't concentrate.	.08	.06	1.30	.420
I feel hopeless.	.20	.06	3.36	.008
How's your day?	.16	.06	2.59	.052
How would you rate your overall physical health today?	.12	.08	1.42	.364

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.24 *Meta-analysis of agreeableness and the variabilities of the DDI items across the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	.18	.11	1.64	.282
I feel sad.	.09	.06	1.44	.356
I feel irritable.	.11	.06	1.77	.233
I enjoy what I am doing.	.12	.06	2.06	.145
I don't care about anything.	.02	.06	.40	.849
I have no appetite during the day.	.05	.06	.80	.670
I worry about sleeping.	.02	.06	.34	.878
I didn't have enough sleep last night.	.15	.06	2.44	.067
I am restless.	.09	.06	1.44	.356
I am tired.	.12	.06	1.97	.169
It is not effortful to do things.	.11	.07	1.54	.319
I feel guilty.	.01	.11	.09	.972
I am doing things at my normal pace.	.06	.08	.67	.731
I feel worthless.	.06	.06	.90	.620
I feel that I can't get anything done.	.12	.07	1.79	.227
I feel that I can't make decisions.	.14	.10	1.40	.374
I can't concentrate.	.07	.06	1.08	.529
I feel hopeless.	.10	.06	1.64	.281
How's your day?	.11	.06	1.85	.209
How would you rate your overall physical health today?	.09	.08	1.12	.510

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 5.25 *Meta-analysis of conscientiousness and the variabilities of the DDI items across the three studies* (*N* = 277)

DDI item	*β*	*SE*	*z*	*p*
I feel happy.	-.01	.11	-.09	.972
I feel sad.	-.10	.06	-1.65	.278
I feel irritable.	-.15	.06	-2.43	.071
I enjoy what I am doing.	-.09	.06	-1.58	.302
I don't care about anything.	-.19	.06	-3.17	.014
I have no appetite during the day.	-.12	.06	-1.98	.167
I worry about sleeping.	-.11	.06	-1.78	.229
I didn't have enough sleep last night.	-.08	.06	-1.34	.400
I am restless.	-.09	.06	-1.46	.347
I am tired.	-.02	.06	-.29	.895
It is not effortful to do things.	-.04	.08	-.48	.819
I feel guilty.	.10	.11	.91	.613
I am doing things at my normal pace.	.02	.08	.26	.909
I feel worthless.	-.13	.06	-2.09	.139
I feel that I can't get anything done.	-.19	.07	-2.62	.048
I feel that I can't make decisions.	-.10	.10	-1.00	.568
I can't concentrate.	-.13	.06	-2.14	.125
I feel hopeless.	-.12	.06	-1.89	.195
How's your day?	-.03	.06	-.47	.820
How would you rate your overall physical health today?	.13	.08	1.62	.286

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

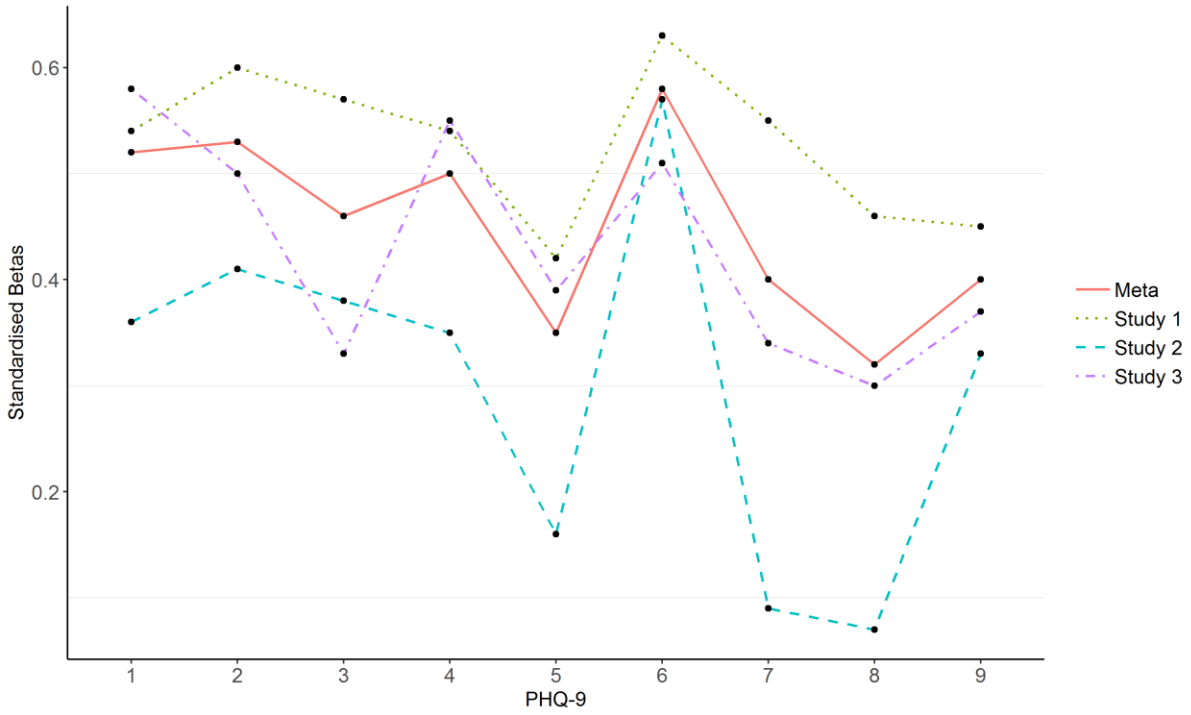


Figure 5.1 The standardized betas of neuroticism when regressing neuroticism on the PHQ-9 items in Studies 1, 2, and 3 and the meta-analysis

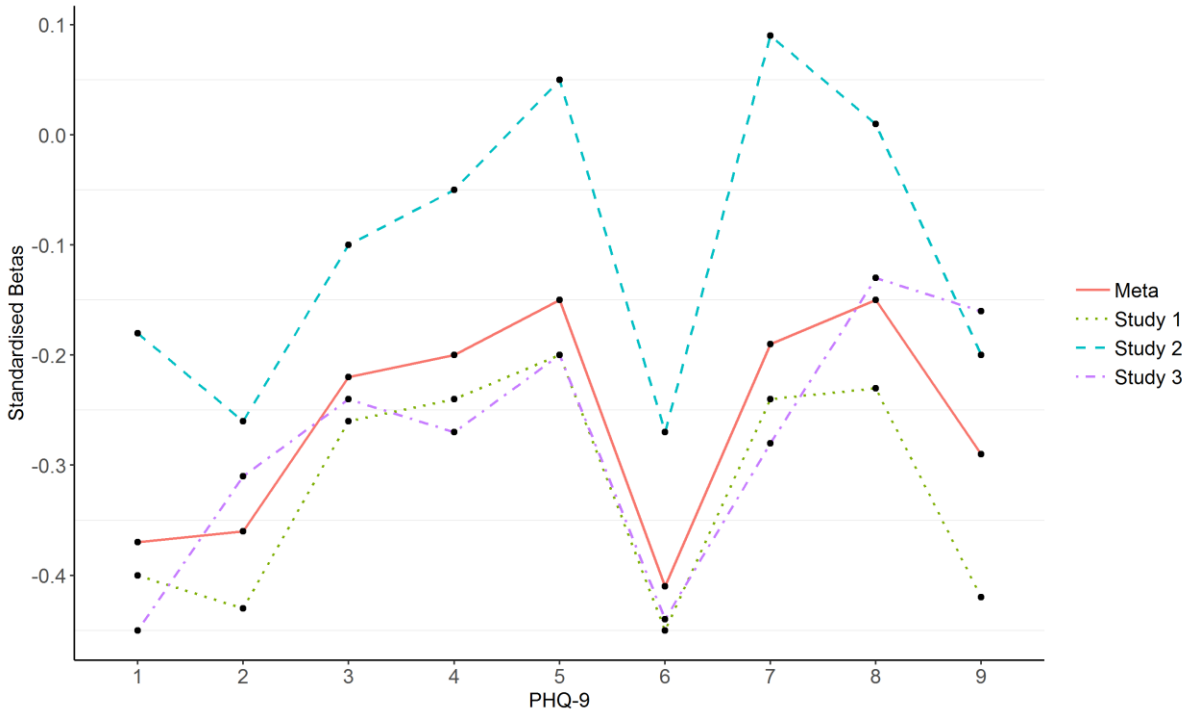


Figure 5.2 The standardized betas of extraversion when regressing extraversion on the PHQ-9 items in Studies 1, 2, and 3 and the meta-analysis

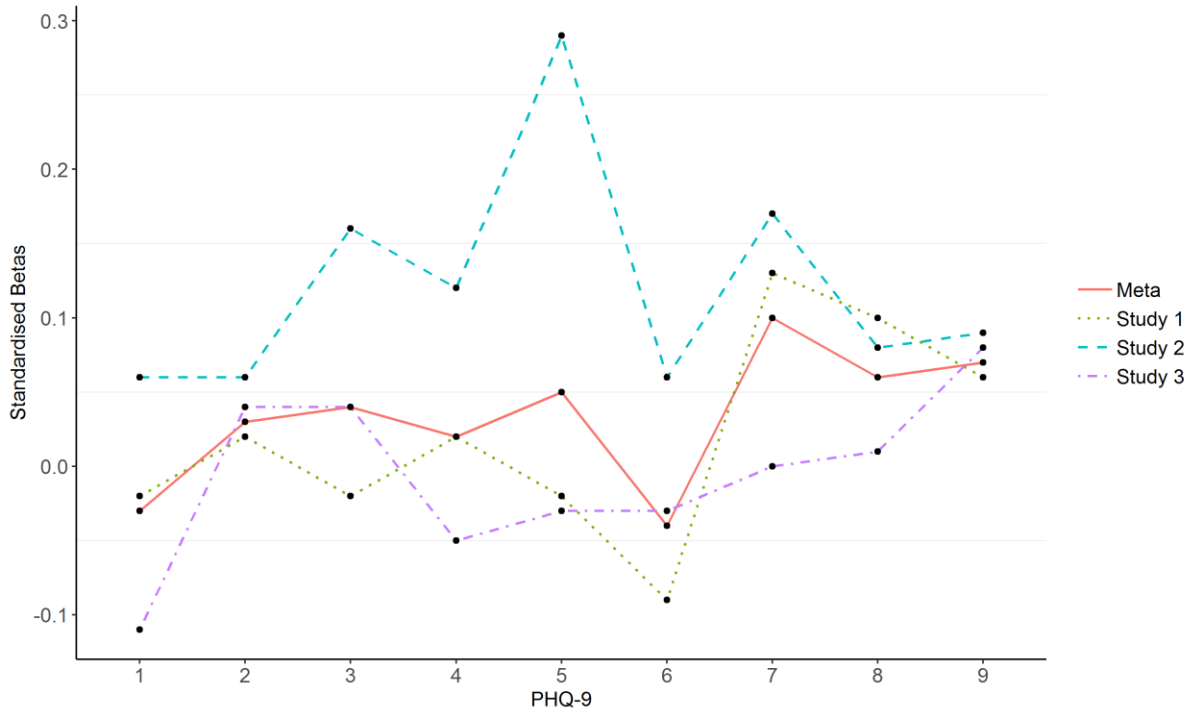


Figure 5.3 The standardized betas of openness when regressing openness on the PHQ-9 items in Studies 1, 2, and 3 and the meta-analysis

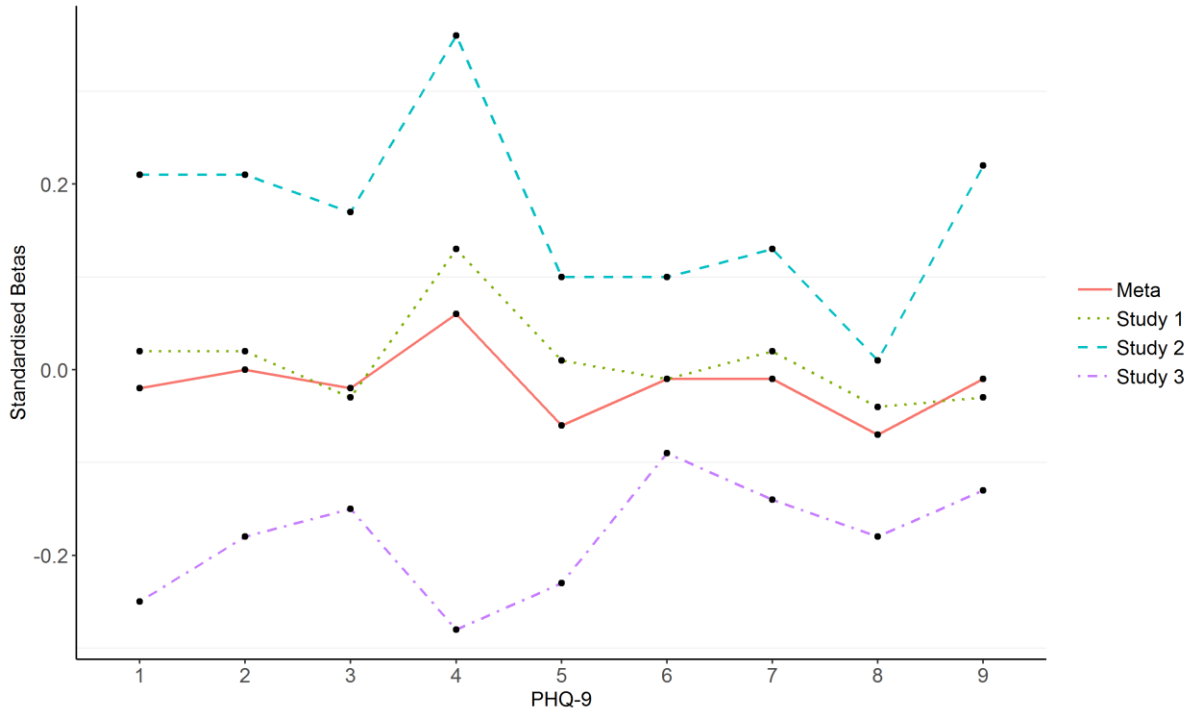


Figure 5.4 The standardized betas of agreeableness when regressing agreeableness on the PHQ-9 items in Studies 1, 2, and 3 and the meta-analysis

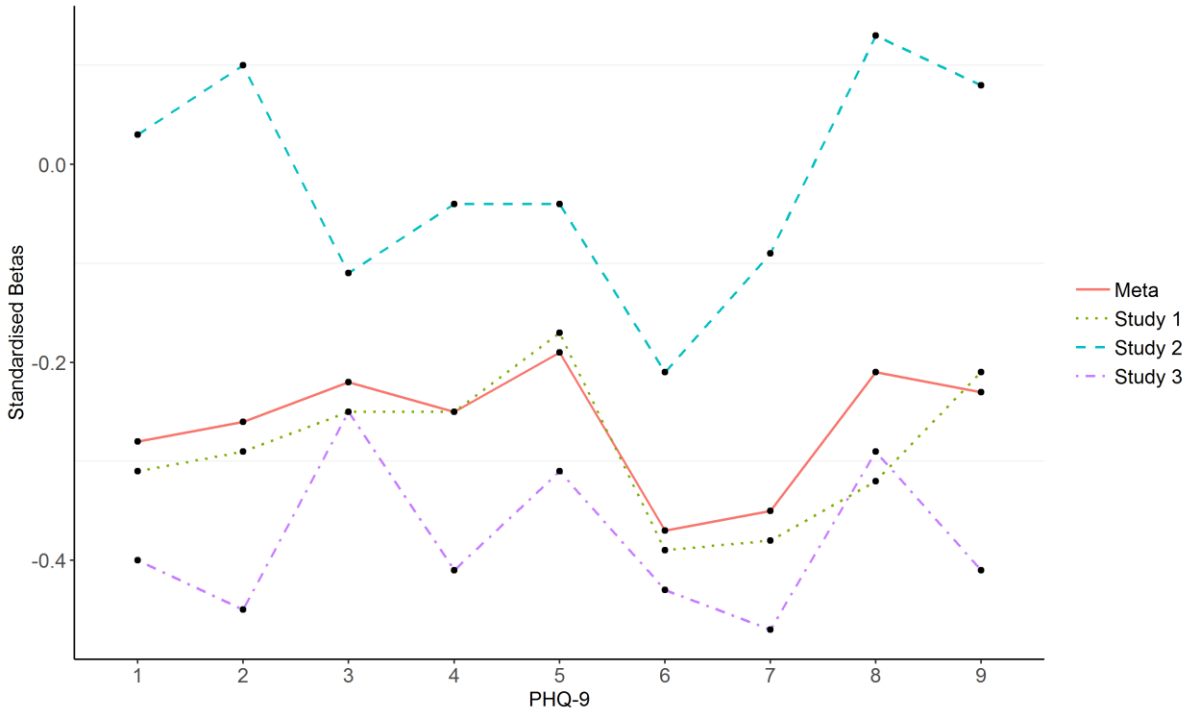


Figure 5.5 The standardized betas of conscientiousness when regressing conscientiousness on the PHQ-9 items in Studies 1, 2, and 3 and the meta-analysis

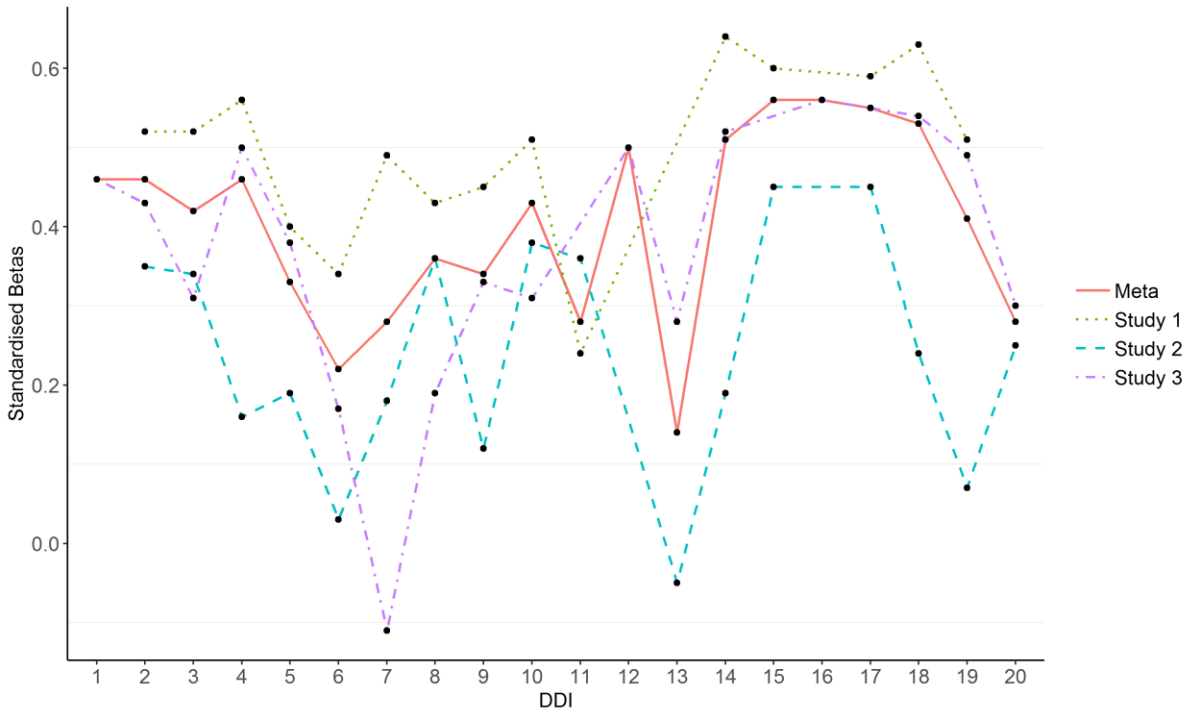


Figure 5.6 The standardized betas of neuroticism when regressing neuroticism on the means of the DDI items in Studies 1, 2, and 3 and the meta-analysis

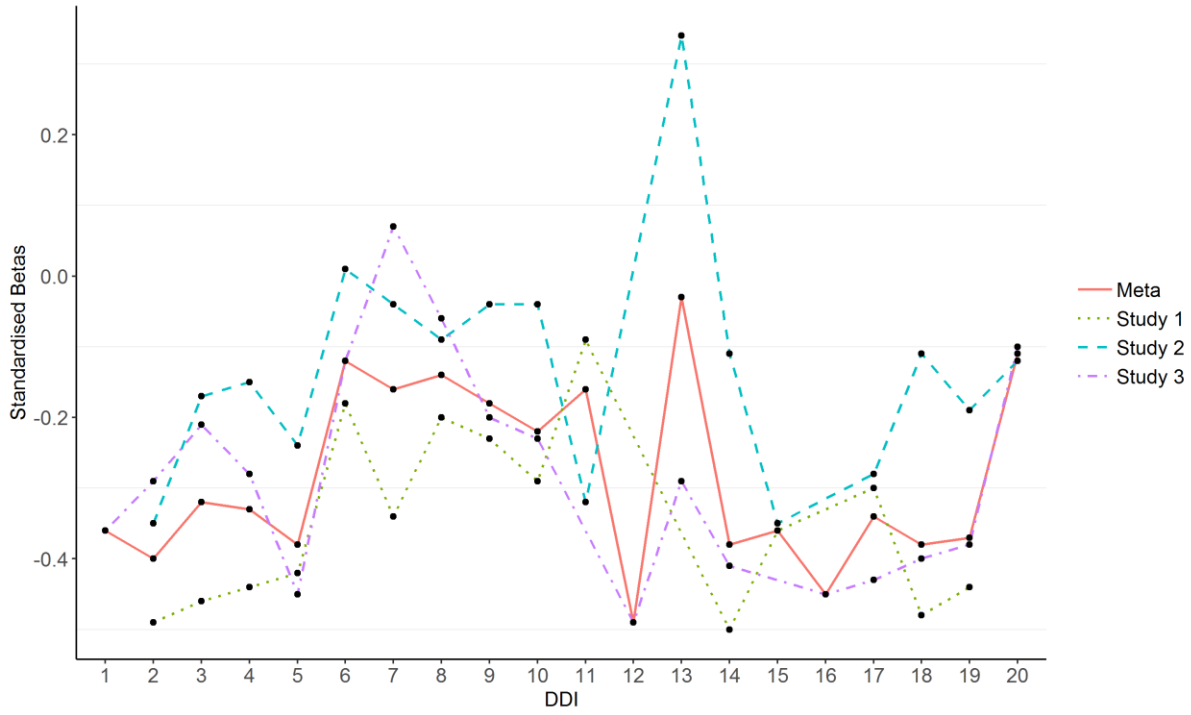


Figure 5.7 The standardized betas of extraversion when regressing extraversion on the means of the DDI items in Studies 1, 2, and 3 and the meta-analysis

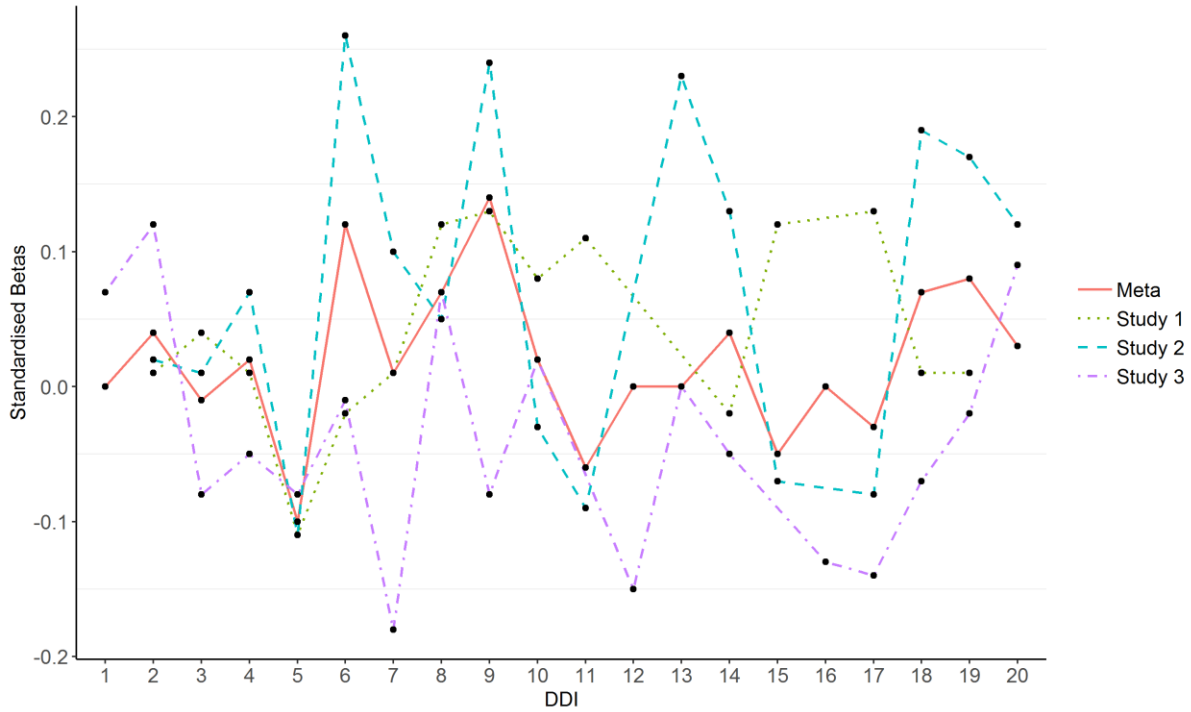


Figure 5.8 The standardized betas of openness when regressing openness on the means of the DDI items in Studies 1, 2, and 3 and the meta-analysis

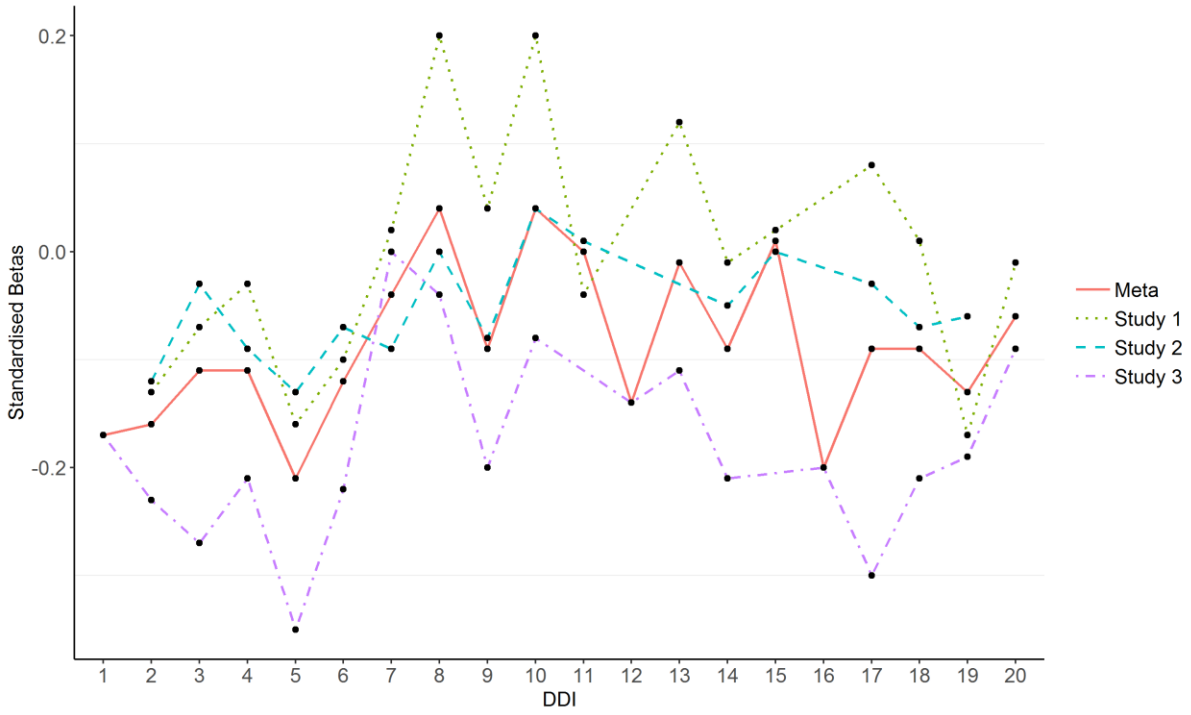


Figure 5.9 The standardized betas of agreeableness when regressing agreeableness on the means of the DDI items in Studies 1, 2, and 3 and the meta-analysis

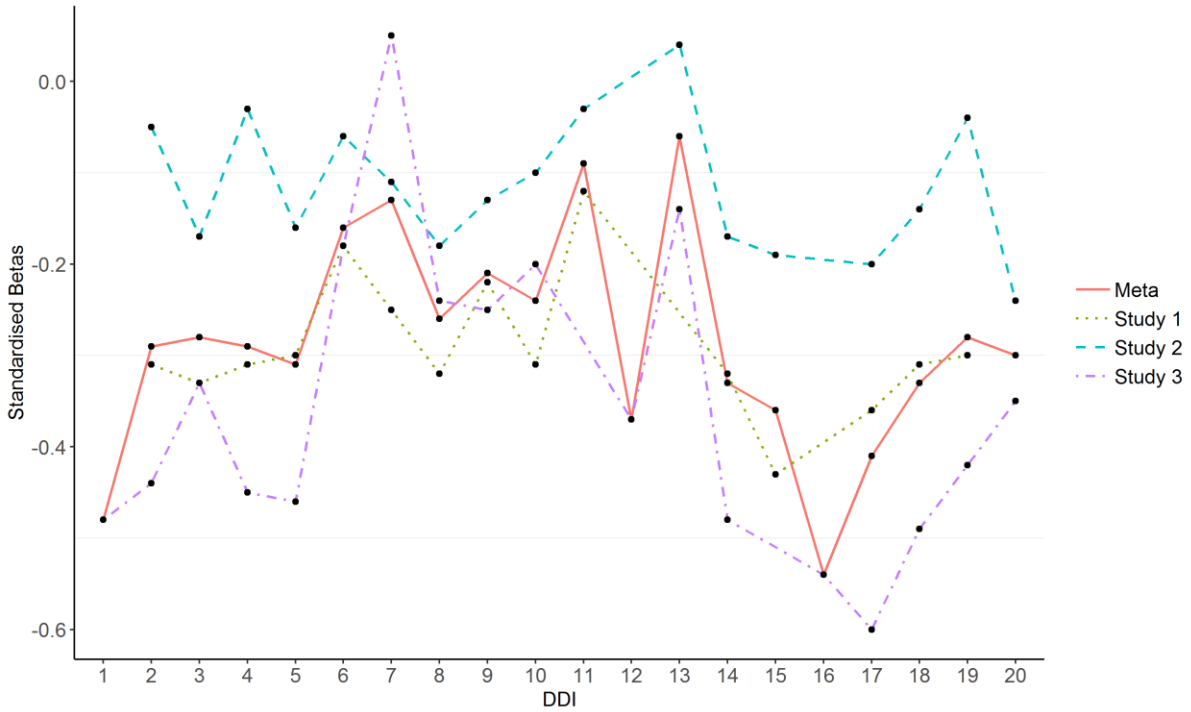


Figure 5.10 The standardized betas of conscientiousness when regressing conscientiousness on the means of the DDI items in Studies 1, 2, and 3 and the meta-analysis

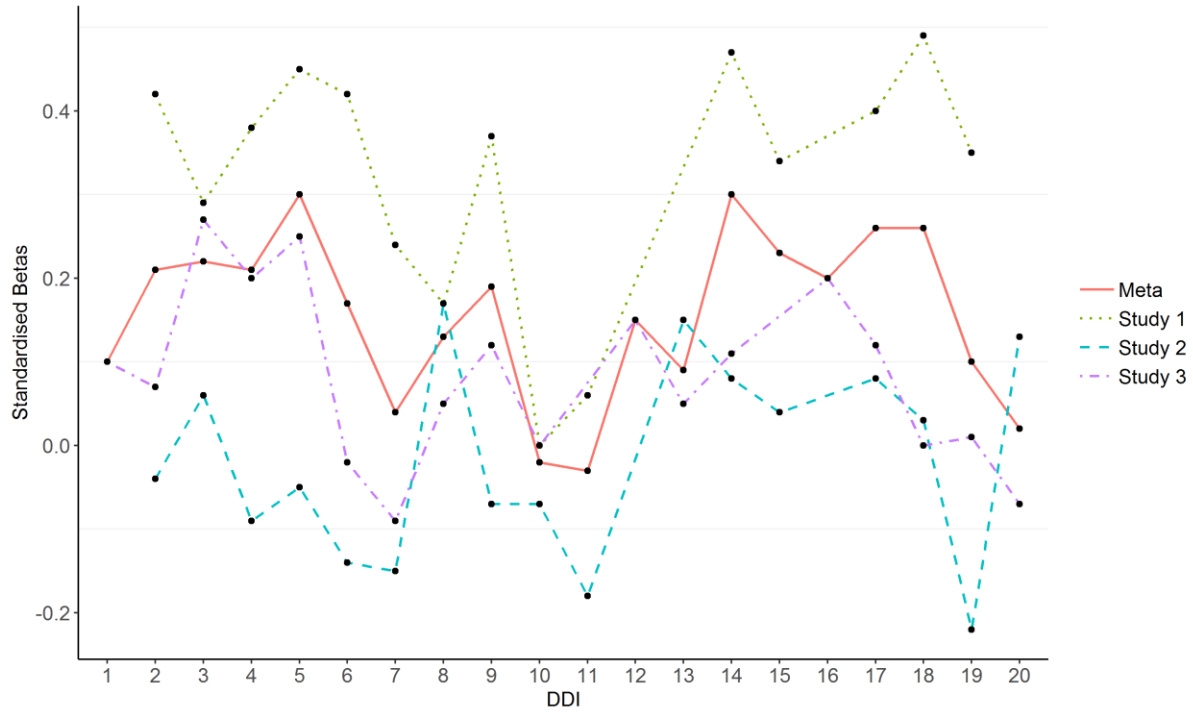


Figure 5.11 The standardized betas of neuroticism when regressing neuroticism on the standard deviations of the DDI items in Studies 1, 2, and 3 and the meta-analysis

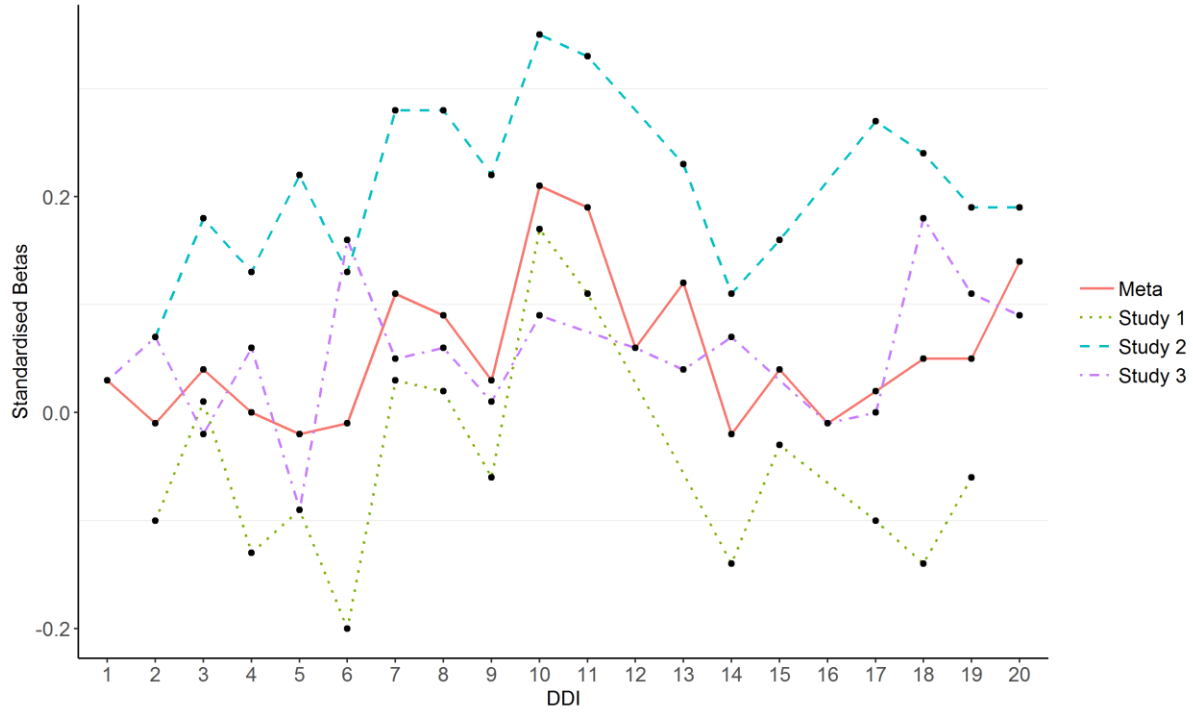


Figure 5.12 The standardized betas of extraversion when regressing extraversion on the standard deviations of the DDI items in Studies 1, 2, and 3 and the meta-analysis

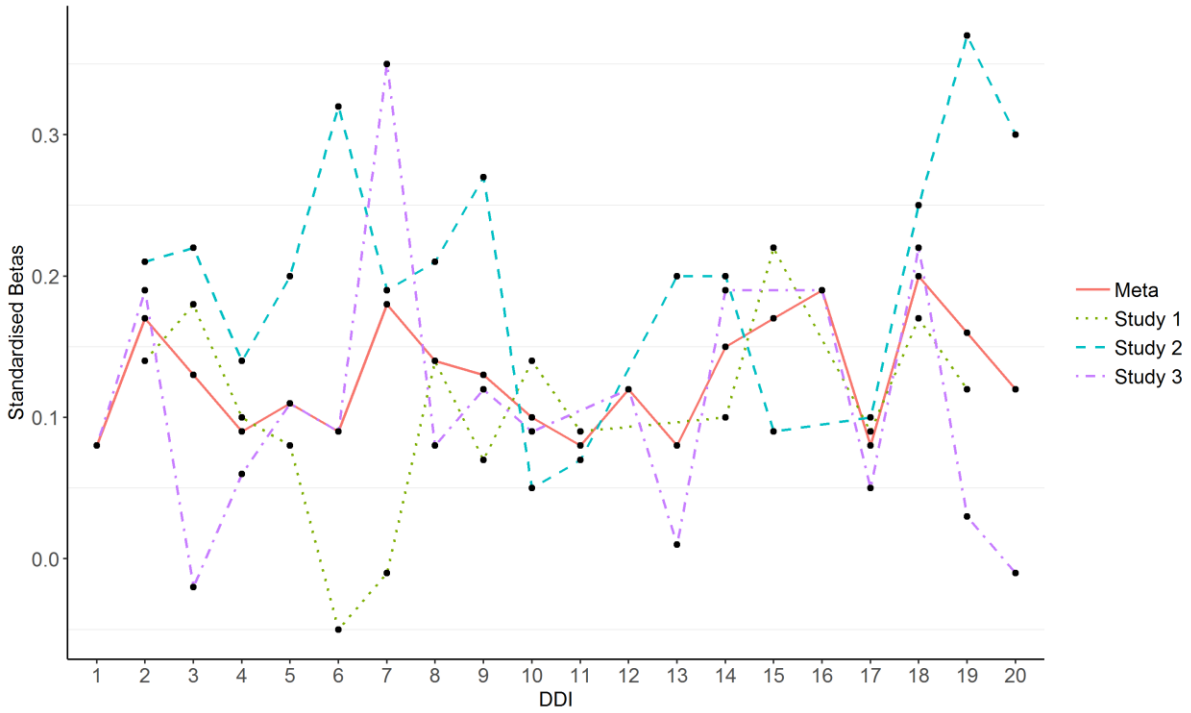


Figure 5.13 The standardized betas of openness when regressing openness on the standard deviations of the DDI items in Studies 1, 2, and 3 and the meta-analysis

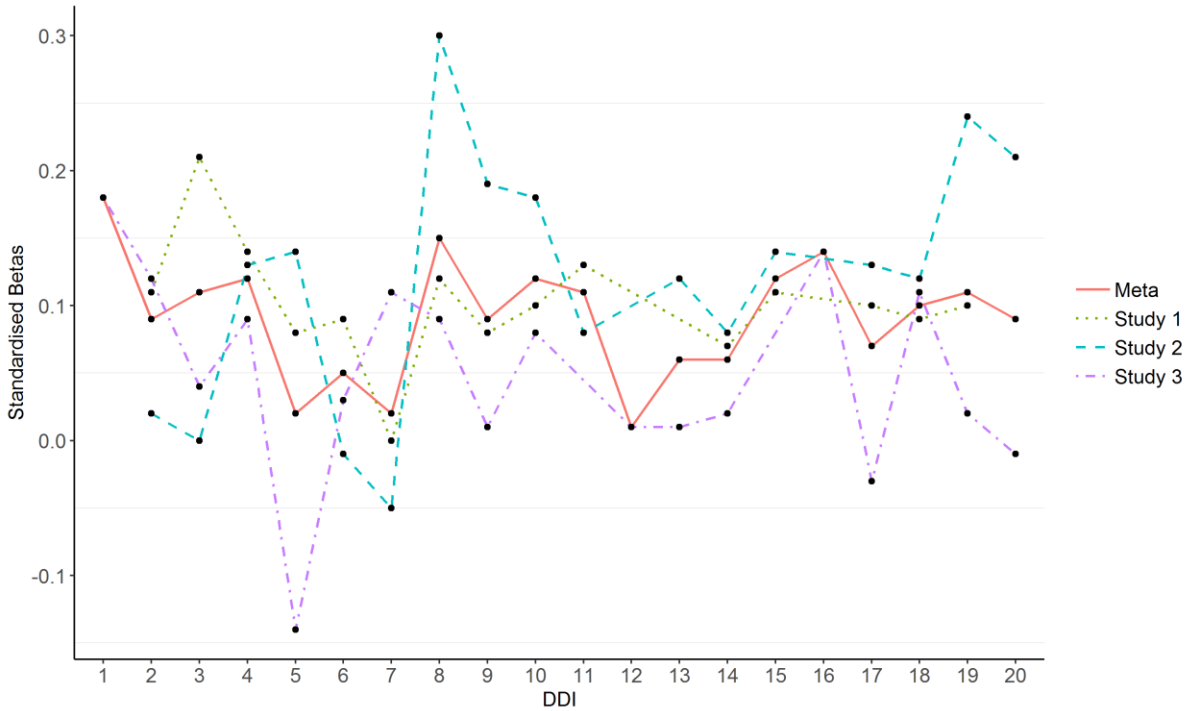


Figure 5.14 The standardized betas of agreeableness when regressing agreeableness on the standard deviations of the DDI items in Studies 1, 2, and 3 and the meta-analysis

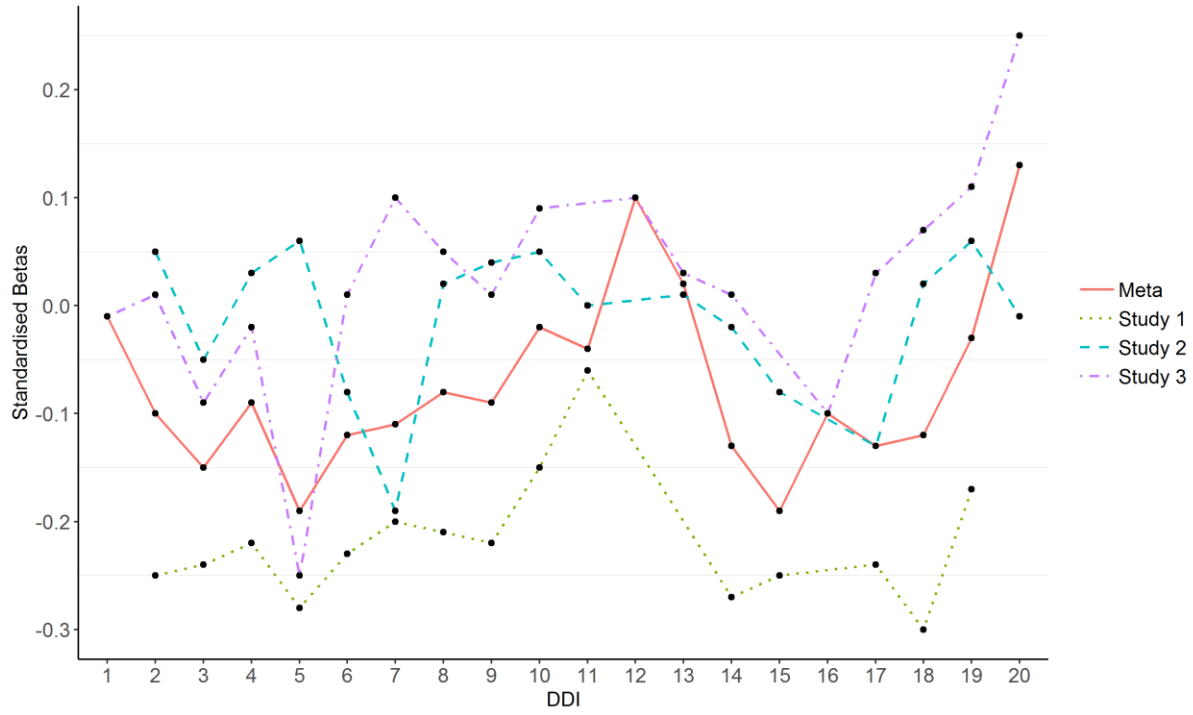


Figure 5.15 The standardized betas of conscientiousness when regressing conscientiousness on the standard deviations of the DDI items in Studies 1, 2, and 3 and the meta-analysis

Discussion

The results from three studies and meta-analysis partially supported H12 – MD severity is associated with high neuroticism, although the links between MD severity and low extraversion and low conscientiousness were not observed in Study 2. H13 described the relationships between MD severity and depression under neuroticism and cheerfulness under extraversion was supported across the three studies. The results also showed the mean momentary ratings (the DDI) were equally reliable as the retrospective ratings (the PHQ-9) and the momentary data could provide more informative insight into the condition under investigation depending on the research questions and the subsequent analyses.

Our finding of neuroticism as the only significant predictor of MD is consistent with the literature (Burcusa & Iacono, 2007; Kendler et al., 2004; Noteboom et al., 2016; Xia et al., 2011). The associations between PHQ-9 score and neuroticism in the three studies and meta-analysis were significant. The mean and

the variability of momentary MD ratings significantly correlated with neuroticism in Study 1 and meta-analysis, but the significant associations were only found in a few DDI items in Studies 2 and 3. The different predictability of personality traits may be explained by unbalanced personality hierarchy and different levels of abstraction in traits as mentioned in Markon et al. (2005). Heterogeneity in MD symptoms might be another possible explanation. More detailed observations into MD symptoms are heterogeneous could be found in the variances in *p*-values and the ranges of betas of items from either the associations between personality traits and facets and the PHQ-9 or DDI items in the meta-analysis. Only some items significantly correlated with the traits neuroticism, extraversion, and conscientiousness, and the facets depression and cheerfulness. The least number of significant links between the traits and the facets were found in the standard deviations of the DDI items. The standardized betas from the best-fit models in the three studies were not comparable because the betas were from different models. In meta-analysis, there were relatively wide ranges of standardized betas between the PHQ-9 items and neuroticism (.26) and extraversion (.28), between the means of the DDI items and neuroticism (.42), extraversion (.46), and conscientiousness (.48), between the standard deviations of the DDI items and neuroticism (.33) and conscientiousness (.32). Together, these may well support the claim of heterogeneity in MD symptoms.

Limitations and future directions

The three studies only tested the relationships between personality traits and facets and variability of MD symptoms. Future studies could look into how personality affect MD symptom stability. Stability covers both dispersion from the baseline and the chronological order of the changes and it might provide more insight into the timing when personality traits and facets start to influence MD symptoms.

Two facets – N1 anxiety and N6 vulnerability – were significantly correlated with the majority or all PHQ-9 items and the mean momentary ratings of the DDI items in the three studies. These two facets may be potentially good targets to be used in future research to disentangle the relationship between neuroticism and

MD. In addition, these two facets have been picked up by other researchers and their relationships with life outcome were reported (W. D. Hill et al., 2019). Two subcategories of neuroticism – anxiety/tension and worry/vulnerability were associated with positive life outcome compare to neuroticism, which was linked to poor life outcome. This contrasted with the positive associations between the two facets and depression. A plausible explanation might be that the general variances across all items measuring neuroticism were removed from the anxiety/tension and worry/vulnerability factors in W. D. Hill et al. (2019) and only the residual variances remained, while in this thesis the general variances were kept in the facets.

The inconsistent findings of insignificant associations between MD severity and low extraversion and low conscientiousness in Study 2 might be caused by a smaller sample size (n = 75) compared to Study 1 (n = 127). However, the sample size of Study 2 is similar to that in Study 3 (n = 78) so sample size might not be a plausible explanation and the numbers of data points of Studies 2 and 3 were 3,955 and 4,297, respectively, which was similar, too. The results might either reflect differences between groups of participants or these two traits might be unstable predictors of MD severity.

Conclusion

Personality trait neuroticism and facets depression and cheerfulness are linked to MD severity as reported in three studies and meta-analysis of the three studies. MD symptoms are heterogeneous.

In next chapter, we will explore the relationship between within- and between-individual differences in MD symptoms on one hand and daily activity level and heart rate variability on the other.

Chapter 6 Daily activity level, heart rate variability, and depression

Introduction

Daily activity level and MD

Benefits of physical activities to MD patients has been widely reported (Mammen & Faulkner, 2013; Saeb et al., 2015; Teychenne et al., 2008). Being physically active – regardless of activity frequency, duration or intensity– reduced the probability of having MD was reported in a review of 27 observational and 40 intervention studies (Teychenne et al., 2008). This review included both cross-sectional and longitudinal studies. However, cross-sectional studies cannot inform causal relationships among the variables. This limits the implications of the results. Mammen and Faulkner (2013) reviewed 30 longitudinal studies and assessed the quality of the methodologies used in these studies. They found physical activities had protective effect against MD. Reciprocal effect between physical activities and MD was observed, too. In another review of 24 studies, people with MD were found to spend less time on physical activities in general and on moderate to vigorous physical activities in particular, but they spent more time on sedentary behaviors than the normal controls (Schuch et al., 2017). A small study using sensors and mobile phone global positioning systems to collect movement-related data such as time spent at home, variability of locations, time spent at various locations, and time spent to travel between locations (Saeb et al., 2015). They found MD severity was associated with total distance of moving. The above reviews supported the upholding role of physical activity in reducing MD symptoms.

Sedentary behavior and health

Sedentary behavior is usually regarded as the opposite of physical activity. Even though the relationship between sedentary behavior and health has been inconclusive, sedentary behaviors is reported as a possible cause of health problems independent of physical activity (de Rezende et al., 2014; Katzmarzyk, 2010). In an overview of 27 systematic reviews of observational studies, various age groups and

types of sedentary behaviors were found to differ in health outcomes (de Rezende et al., 2014). They reported that in children and adolescents, sedentary behavior of TV viewing and screen-time was associated with obesity. In adults, sedentary behaviors of sitting time, time spending on watching TV and watching screens were related with all-cause mortality, cardiovascular disease, and metabolic syndromes. Moderate relationships were found between sedentary behavior and several types of cancer. Their results suggested more research into the relationship between sedentary behavior and health is needed because it has not been well established.

Heart rate variability and MD

Heart rate variability reflects the communication between the central nervous system and the peripheral nervous system – the regulatory signals from the central nervous system to the peripheral nervous system and the feedback from the peripheral nervous system to the central nervous system (Servant et al., 2009). It also indicates how hearts respond to physiological signals such as breathing and blood pressure (Mather & Thayer, 2018). In their study, Mather and Thayer (2018) suggested heart rate variability could enhance brain networks responsible for emotion regulation via modulating the timing of blood flow. In addition, heart rate variability has been linked to self-control in a review of 24 articles including 26 studies (Zahn et al., 2016) and top-down self-regulatory mechanisms in a meta-analysis of 126 studies (Holzman & Bridgett, 2017). Significant, albeit small effect sizes were reported in both reviews. Stronger associations were found in older compared to younger participants (Holzman & Bridgett, 2017). A meta-analysis of heart rate variability in adolescents, young adults, and older adults during social interactions demonstrated heart rate variability decreased during negative social interactions, and people with psychiatric disorders did not have cardiac autonomic flexibility – decreased flexibility when the participants were under stress and increased flexibility during positive social interactions (Shahrestani et al., 2015). People with psychiatric disorders including mood and anxiety disorders and alcohol dependence have low heart rate variability (A. H. Kemp & Quintana, 2013).

MD relates to reduced heart rate variability (Brunoni et al., 2013; A. H. Kemp et al., 2010; Koenig et al., 2016; Nahshoni et al., 2004). An indicator of vagal activity, low resting state high frequency heart rate variability was reported in children and adolescent MD patients (Koenig et al., 2016). In normal controls, no associations between high frequency heart rate variability and MD symptom severity were identified. Declined heart rate variability were also found in adult MD patients in a Brazilian study (Brunoni et al., 2013), in both MD patients who received or who did not receive heart transplants (Nahshoni et al., 2004), and in MD patients with increased MD severity in a meta-analysis of 18 studies (A. H. Kemp et al., 2010).

The presence of comorbidity and subclinical psychiatric disorders demonstrated the currently widely used nosology may not be the optimal framework to diagnose psychiatric disorders (Krueger & Eaton, 2015), thereby demonstrating the necessity of having alternative diagnostic tools such as transdiagnostic tools. High-frequency heart rate variability may be used a transdiagnostic factor in MD diagnosis, because it has been associated with several psychiatric disorders as suggested in a review (Beauchaine & Thayer, 2015). Other transdiagnostic factors include internalizing and externalizing spectra (Krueger & Markon, 2006, 2011) and maladaptive repetitive thought (Kaplan et al., 2018). In addition, heart rate variability seemed to be a stable indicator of MD because it remained the same after transcranial direct current stimulation treatment (Brunoni et al., 2013) and antidepressant treatment (Brunoni et al., 2013; A. H. Kemp et al., 2010). The only exception was tricyclic antidepressant, which decreased heart rate variability (A. H. Kemp et al., 2010).

Life expectancy in MD patients

People with mental disorders on average lived 10 years shorter than those who did not have mental disorders as reported in a systematic review and meta-analysis of 203 studies (Walker et al., 2015). The mortality rate in MD patients has been observed to be higher than the normal population in several reviews and meta-analysis (Chang et al., 2011; Cuijpers et al., 2014; Gilman et al., 2017; Walker et al., 2015). People with several types of serious mental illnesses including

schizophrenia, bipolar disorder, substance use disorder, and MD were found to have a shorter life expectancy compared to the normal population (Chang et al., 2011). A meta-analysis of 293 studies compared the risk of mortality in MD before and after adjusting for publication bias and study quality (Cuijpers et al., 2014). After controlling for these two factors, the risk of mortality in MD was reduced but people with MD still had approximately 50% higher mortality rate than the normal controls. Cuijpers et al. (2014) also observed similar rate of mortality in community-based participants with MD and other MD patients. In a study conducted in Denmark, compared to the general population, men with MD lived 14 years shorter and women with MD lived 10.1 years shorter (Laursen et al., 2016). Even though the influences of MD episodes on the risk of mortality diminished with time, its influence may last as long as 20 years after the latest MD episode (Gilman et al., 2017).

Causes of death in mental disorders

Some studies examined the causes of death in people with mental disorders – whether it being natural (e.g., diseases) or unnatural (e.g., accidents or suicide). Deaths in people with substance abuse and eating disorders could be attributed to natural or unnatural causes (Harris & Barraclough, 1998). While unnatural causes were the primary reason of death among people with schizophrenia and MD. Most of those with intellectual instability and epilepsy died of natural causes. In a review, Walker et al. (2015) reported 67.3% of the cause of death in people with mental disorder was natural and 17.5% was unnatural. In a Swedish cohort study on MD and bipolar disorder, natural causes were the main causes of death (Ösby et al., 2001). Laursen et al. (2016) investigated the causes of death among MD patients in Denmark and found the primary cause of death was natural causes.

Elevated rates of cardiovascular diseases in people with severe MD have been found in several studies of participants from various countries including the U.S. (Saint Onge et al., 2014), Singapore (Ho et al., 2016), and Sweden (Ösby et al., 2001). In the study conducted in the U.S., MD was related to a 43% increase in the

risk of mortality even after controlling for covariates including sociodemographic factors, health behaviors, and health conditions (Saint Onge et al., 2014). In particular, a diagnosis of MD may increase the probability of having cardiovascular disease in people who have and who do not have cardiovascular disease previously by 1.82 and 2.68 times, respectively. In the study of an elderly group of participants in Singapore, both MD and subthreshold depression were linked to risk of mortality (Ho et al., 2016). A small portion of the risk may due to unhealthy behaviors and the majority of it might due to other medical conditions and functional disability. As a result, after controlling for the two variables, the authors still did not find any associations between subthreshold depression and the risk of mortality and MD was still linked to cardiovascular disease and stroke. In the Swedish study, the three leading causes of death were cardiovascular disease, suicide, and cancer in both MD and bipolar disorder patients (Ösby et al., 2001). Suicide was the primary risk of mortality in young patients one year after their diagnoses. Low heart rate variability might implicate the link between MD and cardiovascular mortality via autonomic nerve dysfunction (Carney & Freedland, 2009; Gorman & Sloan, 2000).

Autonomic imbalance might explain the mechanism underlying cardiovascular diseases as reported in a review (Thayer et al., 2010). Autonomic imbalance describes a hyperactive sympathetic system and a hypoactive parasympathetic system, and the potential consequences may be early ageing and diseases. This review analyzed studies on several risk factors of cardiovascular diseases including hypertension, diabetes, smoking, physical inactivity, overweight, age, family history, and work stress. Thayer et al. (2010) suggested heart rate variability may be used as an indicator of autonomic imbalance. However, their claim was challenged by Kluttig, Kuss, and Greiser (2010) for ignoring studies reporting the opposite or neutral findings. Thayer, Yamamoto, and Brosschot (2010a) later replied Kluttig et al. (2010) and stressed their review was not exhaustive and the presence of other risk factors may influence the results of the studies mentioned in Kluttig et al. (2010). This may be of concern especially when the sample population have risk factors with similar frequencies. Therefore,

distinguishing the effects of different risk factors might be difficult. Despite many studies supported the link between heart rate variability and MD, there were still objections (Borrione et al., 2018). Different associations between heart rate variability and MD symptoms may be a possible explanation; therefore, Borrione et al. (2018) tested this and found three MD symptoms – feeling guilty, loss of interest or pleasure, and psychomotor retardation – were associated with heart rate variability. The disparities between studies might arise because of varying symptom coverages in commonly used MD assessments (Fried, 2017; Fried, van Borkulo, et al., 2016). Studies reported associations between heart rate variability and MD symptoms might have adopted MD assessments including symptoms related to heart rate variability while studies did not find these associations might have used other MD assessments did not include these symptoms that correlated with heart rate variability.

Heterogeneous expressions of MD symptoms may also result from within- or between-individual differences because variances were found in results obtained from analyses of between- and within-individual differences (A. J. Fisher et al., 2018; Hamaker, 2012; Kanning et al., 2013; Laukka et al., 2018). Discrepancies between within- and between-individual differences in activity level and affect has been reported in a review (Kanning et al., 2013). The results obtained from between-individual analyses might diverge from those found in within-individual analyses (Hamaker, 2012). Deviances between within- and between-individual differences were found in the cognitive performance of older adults receiving tests of anxiety and depression (Laukka et al., 2018). The influences of within-individual differences on cognitive performance were huge for depression generally while between-individual differences affected greatly for anxiety.

The study

This chapter explores the relationships between two MD measures – between- and within-individual differences in MD symptoms – and activity levels and heart rate variabilities. Instead of self-reports, activity sensors were used to measure and to record physical activity level in healthy participants. Although self-

reports with short recall periods may show greater accuracy than those with long recall periods (Short et al., 2009), they are still subject to the possible influences of memory decay or memory bias. In addition, self-reported activity levels are unstable and relatively inaccurate in relation to sensor-recorded data as reported in a review of 187 papers (Prince et al., 2008). Therefore, wearable activity sensors, which have greater accuracy than self-reported activity levels, were used in data collection. Heart rate variability was recorded along with physical activity level. Relationships between MD symptoms and daily activity level and between MD symptoms and heart rate variability were examined in one study.

We hypothesize that depression would appear as an etiologically homogeneous entity with all MD symptoms relating to activity levels in the same way – lower activity level would coincide with higher ratings of MD symptoms – and that these associations would exist for within-individual MD symptoms (measurement occasions with higher activity would also show lower MD symptom scores) and for daily activity level (H14). Similar homogeneous relationships of lower hear rate variability and higher ratings of MD symptoms would be found in within-individual MD symptoms and heart rate variability (H15).

Materials and Method

The same participant, materials, and procedure as described in Study 3 (Chapters 2 to Chapter 5) were used. Three-dimensional movement acceleration was used to calculate activity levels because it could distinguish activity types, intensity, frequency, pattern, and duration of activity (Berlin et al., 2006; Shephard & Tudor-Locke, 2016). The acceleration measurement is generated every minute. The signals from the three axes are firstly bandpass filtered to remove the offset from gravity and irrelevant high frequency contents (movisens GmbH, 2019). The vector magnitude of the output signals is calculated using the following formulae:

$$ma_i = \sqrt{ax^2{}_{bp} + ay^2{}_{bp} + az^2{}_{bp}}$$

The output values are calculated by averaging the means of all collected measurements in the interval.

Heart rate variability was measured using rMSSD, which is an indicator of vagus-mediated heart rate variability (DeGiorgio et al., 2010). It is the root mean square of successive difference in heartbeats (movisens GmbH, 2019; Shaffer & Ginsberg, 2017).

Results

Multilevel models were used to test the hypotheses. All continuous variables were grand-mean centered. The average activity levels and heart rate variabilities 30, 60, and 120 minutes before and after the momentary measurements of MD symptoms were the outcome variables in each multilevel model. The within- and between-individual MD symptom differences and the covariates – age, gender, educational attainment, marital status, and employment status were the fixed factors. Individual participant was the random intercept factor. The within-individual differences in MD symptoms were calculated by standardizing the momentary MD symptom ratings. The standardized values have a mean of 0 and a standard deviation of 1. The between-individual differences were the means of the momentary MD symptoms ratings for each participant. The R code of the multilevel model was in Appendix B. The same as in Chapters 3–5, age and educational attainment were continuous and gender, marital status, and employment status were categorical. Marital status and employment status were collapsed into fewer levels to avoid issues such as collinearity or undermine power. Marital status was collapsed into two levels of single, divorced, and widowed and in a relationship and married. Employment status was collapsed into two levels of employed, self-employed, and full-time student and part-time employed, retired, and unemployed. To tackle the problem of multiple comparison, all *p*-value were corrected using false discovery rate.

Daily activity level

A total of 4,297 observations from 78 participants were collected and analyzed. Significant relationships between activity levels and MD symptoms were observed both in within- and between-individual differences. In general, greater

standardized betas were observed in within- than in between-individual differences in MD symptoms in activity levels measured before and after participants rated their momentary MD ratings. The standardized betas fluctuated more in between-individual differences than in within-individual differences. There were fewer significant associations between MD symptoms and activity level for the activity levels measured after than before the momentary MD ratings were given. Significant between-individual differences in "*I feel happy*", "*I am doing thing at my normal pace*", and "*I feel worthless*" were found in the mean activity levels measured 30, 60, and 120 minutes before participants rated these MD symptoms. Also, significantly between-individual differences were observed in three DDI items and the mean activity levels either measured 30, 60, or 120 minutes before these three DDI items were rated. Significant within-individual differences in "*I feel happy*", "*I don't care about anything*", and "*I can't concentrate*" were found in the mean activity levels measured 30, 60, and 120 minutes after participants rated these DDI items. Within-individual differences in three DDI items were significantly related to the mean activity levels measured 30, 60, or 120 minutes before these DDI items. Tables 6.1–6.6 show the associations between within- and between-individual differences in MD symptoms and the mean activity levels recorded 30, 60, and 120 minutes before and after participants rated MD symptoms.

The sparse significant links between MD symptoms and activity levels showed heterogeneity in MD symptoms. The variances between MD symptoms were more prominent in activity levels measured 120 minutes before the momentary MD ratings for between-individual differences as observed in the ranges of standardized betas. The standardized betas of the items in the DDI were either negative or close to zero, implying associations between low activity level and both between- and within-individual differences in MD symptom ratings. Therefore, H14 was rejected.

Table 6.1 *Associations between mean activity levels measured 30 minutes before rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.11	-.08	.03	.02	-.17	-.11	-.05	-.04	.020	< .001
I feel sad.	-.09	-.06	.04	.02	-.16	-.09	-.02	-.02	.121	.033
I feel irritable.	-.05	-.01	.03	.02	-.11	-.05	.02	.02	.473	.828
I enjoy what I am doing.	-.09	-.04	.04	.02	-.15	-.08	-.02	-.01	.121	.121
I don't care about anything.	-.12	-.06	.04	.02	-.19	-.10	-.06	-.03	.020	< .001
I have no appetite during the day.	-.10	-.03	.04	.03	-.18	-.10	-.02	.03	.132	.668
I worry about sleeping.	.01	.02	.04	.03	-.08	-.05	.09	.08	.962	.912
I didn't have enough sleep last night.	-.05	.02	.05	.03	-.14	-.05	.05	.08	.692	.884
I am restless.	-.05	-.02	.04	.02	-.13	-.06	.02	.01	.475	.509
I am tired.	-.06	-.04	.04	.02	-.12	-.07	.01	-.01	.394	.151
I feel guilty.	-.08	-.05	.04	.02	-.15	-.09	-.01	-.02	.169	.054
I am doing things at my normal pace.	-.11	.00	.04	.02	-.19	-.03	-.04	.04	.041	.990
I feel worthless.	-.11	-.02	.04	.02	-.18	-.06	-.04	.01	.047	.549
I feel that I can't make decisions.	-.09	-.04	.04	.02	-.16	-.07	-.01	.00	.174	.223
I can't concentrate.	-.06	-.06	.04	.02	-.13	-.10	.01	-.03	.348	< .001
I feel hopeless.	-.07	-.02	.04	.02	-.14	-.05	-.01	.02	.201	.606
How's your day?	-.08	-.07	.04	.03	-.15	-.12	-.01	-.01	.201	.117
How would you rate your overall physical health today?	-.05	-.06	.04	.03	-.13	-.11	.04	.00	.636	.200

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Table 6.2 *Associations between mean activity levels measured 60 minutes before rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.11	-.06	.04	.02	-.18	-.09	-.05	-.02	.041	.033
I feel sad.	-.08	-.05	.04	.02	-.16	-.08	-.01	-.01	.223	.103
I feel irritable.	-.02	-.03	.04	.02	-.10	-.06	.05	.01	.861	.463
I enjoy what I am doing.	-.07	-.04	.04	.02	-.14	-.08	.01	-.01	.334	.121
I don't care about anything.	-.11	-.07	.04	.02	-.19	-.11	-.04	-.04	.054	< .001
I have no appetite during the day.	-.11	-.03	.04	.03	-.19	-.10	-.03	.03	.117	.660
I worry about sleeping.	-.04	.01	.05	.04	-.13	-.06	.06	.08	.784	.960
I didn't have enough sleep last night.	.00	.00	.05	.03	-.09	-.05	.09	.06	.974	.973
I am restless.	-.02	-.03	.04	.02	-.10	-.07	.07	.01	.918	.340
I am tired.	-.04	-.05	.04	.02	-.11	-.09	.04	-.02	.667	.047
I feel guilty.	-.07	-.06	.04	.02	-.14	-.09	.00	-.02	.325	.033
I am doing things at my normal pace.	-.16	.00	.04	.02	-.23	-.04	-.08	.03	< .001	.960
I feel worthless.	-.14	-.01	.04	.02	-.21	-.05	-.06	.03	.020	.901
I feel that I can't make decisions.	-.11	-.04	.04	.02	-.19	-.08	-.03	-.01	.090	.132
I can't concentrate.	-.06	-.06	.04	.02	-.13	-.09	.02	-.02	.423	.020
I feel hopeless.	-.07	-.03	.04	.02	-.14	-.07	.00	.01	.305	.345
How's your day?	-.09	-.07	.04	.03	-.17	-.13	-.01	-.01	.199	.137
How would you rate your overall physical health today?	-.06	-.08	.05	.03	-.15	-.14	.03	-.02	.493	.121

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Table 6.3 *Associations between mean activity levels measured 120 minutes before rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.14	-.06	.05	.02	-.22	-.10	-.05	-.03	.047	.020
I feel sad.	-.09	-.05	.05	.02	-.18	-.09	.01	-.01	.340	.082
I feel irritable.	-.02	-.04	.05	.02	-.11	-.08	.07	.00	.911	.181
I enjoy what I am doing.	-.07	-.06	.05	.02	-.16	-.10	.02	-.02	.463	.020
I don't care about anything.	-.11	-.07	.05	.02	-.21	-.11	-.02	-.04	.155	< .001
I have no appetite during the day.	-.16	-.03	.05	.03	-.25	-.09	-.06	.03	.041	.667
I worry about sleeping.	-.09	.03	.06	.03	-.21	-.03	.03	.10	.473	.668
I didn't have enough sleep last night.	.01	.01	.05	.03	-.07	-.04	.10	.06	.936	.912
I am restless.	-.01	-.04	.05	.02	-.11	-.07	.10	.00	.960	.266
I am tired.	-.06	-.03	.05	.02	-.15	-.07	.04	.01	.580	.348
I feel guilty.	-.06	-.06	.05	.02	-.15	-.09	.03	-.02	.548	.033
I am doing things at my normal pace.	-.23	-.01	.05	.02	-.32	-.05	-.14	.03	< .001	.904
I feel worthless.	-.20	-.01	.05	.02	-.29	-.04	-.11	.03	< .001	.922
I feel that I can't make decisions.	-.19	-.04	.05	.02	-.28	-.08	-.09	.00	< .001	.208
I can't concentrate.	-.07	-.05	.05	.02	-.16	-.09	.02	-.02	.441	.041
I feel hopeless.	-.07	-.03	.04	.02	-.15	-.06	.01	.01	.389	.463
How's your day?	-.10	-.08	.05	.03	-.20	-.14	.00	-.01	.296	.121
How would you rate your overall physical health today?	-.08	-.08	.06	.03	-.20	-.15	.03	-.02	.473	.103

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Table 6.4 *Associations between mean activity levels measured 30 minutes after rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.08	-.04	.03	.02	-.15	-.08	-.02	.00	.121	.201
I feel sad.	-.08	-.05	.04	.02	-.15	-.09	-.02	-.01	.151	.121
I feel irritable.	-.04	.01	.03	.02	-.10	-.03	.03	.05	.622	.918
I enjoy what I am doing.	-.07	.00	.03	.02	-.14	-.04	-.01	.03	.196	.960
I don't care about anything.	-.10	-.01	.04	.02	-.17	-.05	-.03	.03	.074	.918
I have no appetite during the day.	.02	-.05	.04	.03	-.05	-.10	.09	.01	.884	.328
I worry about sleeping.	-.01	.00	.04	.03	-.08	-.06	.07	.05	.959	.974
I didn't have enough sleep last night.	-.03	.00	.04	.03	-.11	-.06	.06	.07	.872	.960
I am restless.	-.05	.04	.04	.02	-.13	.00	.02	.08	.468	.201
I am tired.	-.03	-.06	.03	.02	-.09	-.09	.04	-.02	.764	.047
I feel guilty.	-.07	-.03	.04	.02	-.13	-.07	.00	.01	.294	.339
I am doing things at my normal pace.	-.06	.04	.04	.02	-.13	.00	.02	.08	.423	.214
I feel worthless.	-.09	-.03	.04	.02	-.16	-.07	-.02	.01	.142	.423
I feel that I can't make decisions.	-.05	.01	.04	.02	-.13	-.03	.02	.05	.463	.912
I can't concentrate.	-.02	-.01	.04	.02	-.10	-.05	.05	.02	.900	.785
I feel hopeless.	-.05	.00	.04	.02	-.13	-.04	.02	.03	.473	.959
How's your day?	.02	-.02	.03	.02	-.04	-.06	.08	.02	.810	.722
How would you rate your overall physical health today?	.05	-.01	.04	.02	-.02	-.06	.12	.03	.463	.835

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Table 6.5 *Associations between mean activity levels measured 60 minutes after rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.07	-.03	.04	.02	-.14	-.07	-.01	.01	.214	.463
I feel sad.	-.07	-.04	.04	.02	-.14	-.08	.00	.00	.311	.170
I feel irritable.	-.03	.02	.04	.02	-.10	-.02	.03	.06	.684	.680
I enjoy what I am doing.	-.07	.00	.04	.02	-.14	-.04	.00	.04	.328	.967
I don't care about anything.	-.12	.00	.04	.02	-.19	-.04	-.05	.04	.041	.959
I have no appetite during the day.	.07	-.03	.04	.03	-.01	-.09	.15	.02	.336	.487
I worry about sleeping.	-.01	-.02	.04	.03	-.09	-.07	.07	.03	.959	.767
I didn't have enough sleep last night.	.01	-.01	.05	.03	-.08	-.06	.10	.05	.960	.960
I am restless.	-.05	.07	.04	.02	-.13	.04	.03	.11	.556	< .001
I am tired.	-.03	-.07	.04	.02	-.10	-.11	.05	-.03	.828	< .001
I feel guilty.	-.06	-.02	.04	.02	-.14	-.06	.01	.02	.348	.660
I am doing things at my normal pace.	-.05	.03	.04	.02	-.13	-.01	.03	.07	.509	.346
I feel worthless.	-.09	-.02	.04	.02	-.17	-.07	-.01	.02	.196	.580
I feel that I can't make decisions.	-.05	.01	.04	.02	-.13	-.03	.03	.05	.567	.900
I can't concentrate.	-.01	.00	.04	.02	-.09	-.04	.08	.03	.960	.960
I feel hopeless.	-.05	-.01	.04	.02	-.13	-.05	.03	.03	.606	.912
How's your day?	.04	-.03	.03	.02	-.02	-.07	.10	.01	.580	.473
How would you rate your overall physical health today?	.03	-.04	.04	.02	-.04	-.08	.10	.01	.723	.339

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Table 6.6 *Associations between mean activity levels measured 120 minutes after rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.08	-.01	.04	.02	-.16	-.04	.00	.03	.328	.922
I feel sad.	-.08	-.03	.05	.02	-.17	-.06	.01	.01	.328	.493
I feel irritable.	-.06	.02	.04	.02	-.14	-.02	.02	.06	.468	.606
I enjoy what I am doing.	-.07	.01	.04	.02	-.16	-.03	.01	.04	.339	.947
I don't care about anything.	-.14	-.01	.05	.02	-.22	-.05	-.05	.03	.054	.912
I have no appetite during the day.	.13	-.05	.05	.03	.03	-.11	.23	.01	.132	.386
I worry about sleeping.	.02	-.01	.06	.03	-.09	-.07	.13	.05	.918	.960
I didn't have enough sleep last night.	.01	-.03	.05	.03	-.08	-.09	.11	.02	.959	.567
I am restless.	-.07	.08	.05	.02	-.17	.04	.02	.12	.423	< .001
I am tired.	-.02	-.10	.04	.02	-.10	-.14	.07	-.06	.918	< .001
I feel guilty.	-.08	-.02	.05	.02	-.17	-.05	.01	.02	.328	.784
I am doing things at my normal pace.	.00	.03	.05	.02	-.09	-.01	.10	.07	.974	.423
I feel worthless.	-.05	-.02	.05	.02	-.14	-.06	.05	.03	.680	.778
I feel that I can't make decisions.	.01	.02	.05	.02	-.08	-.02	.11	.06	.934	.580
I can't concentrate.	.01	.00	.05	.02	-.09	-.03	.10	.04	.960	.960
I feel hopeless.	-.05	-.01	.05	.02	-.15	-.04	.05	.03	.668	.922
How's your day?	.03	-.04	.03	.02	-.03	-.08	.09	.00	.660	.264
How would you rate your overall physical health today?	.03	-.05	.04	.02	-.04	-.09	.10	-.01	.767	.170

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Heart rate variability

There were 60 participants completed 3,111 measurements of heart rate variability. The results showed no significant between-individual differences. But the standardized betas changed more in between-individual differences compared to within-individual differences. Within-individual differences in heart rate variability measured before and after the momentary ratings were similar but the standardized betas of between-subject differences in heart rate variability measured before the momentary ratings were smaller than those measured after the momentary ratings. Heart rate variabilities measured 30, 60, and 120 minutes before and 60 minutes after participants rated their levels of concentration were significantly related to their ability to concentrate. Also, doing things on one's own pace was related to heat rate variability measured 30 minutes before the participants rated their pace of doing things. The associations between within- and between-individual differences in MD symptoms and the mean heart rate variability recorded 30, 60, and 120 minutes before and after participants rated MD symptoms were shown in Tables 6.7–6.12.

Much less significant associations between both within- and between-individual differences in MD symptoms were observed in heart rate variability compared to activity levels. The standardized betas showed low heart rate variability coincided with high ratings in between-individual differences in MD symptoms while some positive betas in both within- and between-individual differences in MD symptoms revealed ambiguous results. Limited number of significant associations, too, demonstrated MD symptoms as represented by the DDI items are heterogeneous. In addition, the ranges of standardized betas of between-individual differences in MD symptoms for all activity levels were relatively large, indicating MD symptom heterogeneity. H15 was partially rejected.

Table 6.7 *Associations between mean heart rate variability measured 30 minutes before rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.16	.02	.12	.03	-.38	-.03	.06	.07	.475	.757
I feel sad.	-.08	.02	.12	.03	-.31	-.03	.14	.07	.828	.764
I feel irritable.	.16	.00	.11	.03	-.04	-.06	.37	.05	.456	.960
I enjoy what I am doing.	.01	.03	.12	.03	-.22	-.02	.24	.08	.974	.493
I don't care about anything.	-.07	-.01	.13	.03	-.31	-.06	.17	.04	.884	.912
I have no appetite during the day.	.07	-.03	.20	.06	-.29	-.15	.43	.09	.918	.901
I worry about sleeping.	-.07	.00	.18	.07	-.39	-.14	.25	.13	.918	.979
I didn't have enough sleep last night.	.01	-.03	.12	.05	-.22	-.12	.24	.07	.974	.900
I am restless.	.14	.04	.13	.03	-.10	-.01	.39	.09	.606	.336
I am tired.	.03	.00	.12	.03	-.20	-.06	.26	.05	.950	.960
I feel guilty.	-.06	.00	.12	.03	-.29	-.05	.17	.05	.911	.974
I am doing things at my normal pace.	-.11	.08	.12	.03	-.33	.03	.11	.13	.712	.047
I feel worthless.	-.02	-.04	.12	.03	-.25	-.10	.20	.01	.960	.382
I feel that I can't make decisions.	-.09	.05	.12	.03	-.31	.00	.14	.10	.812	.200
I can't concentrate.	-.05	.09	.12	.02	-.28	.04	.18	.14	.912	< .001
I feel hopeless.	-.07	-.03	.12	.03	-.29	-.09	.15	.02	.875	.518
How's your day?	-.11	.00	.16	.07	-.40	-.13	.19	.14	.828	.974
How would you rate your overall physical health today?	.02	.06	.20	.07	-.33	-.07	.37	.19	.974	.671

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Table 6.8 *Associations between mean heart rate variability measured 60 minutes before rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.16	.00	.12	.03	-.39	-.05	.06	.05	.475	.973
I feel sad.	-.09	.01	.12	.03	-.32	-.04	.13	.07	.784	.884
I feel irritable.	.16	-.01	.12	.03	-.05	-.06	.37	.04	.473	.900
I enjoy what I am doing.	.01	.03	.13	.03	-.22	-.02	.25	.07	.967	.660
I don't care about anything.	-.08	-.01	.13	.02	-.32	-.05	.16	.04	.872	.936
I have no appetite during the day.	.10	-.02	.21	.06	-.28	-.13	.48	.08	.911	.911
I worry about sleeping.	-.08	.01	.19	.06	-.43	-.12	.26	.13	.912	.960
I didn't have enough sleep last night.	.05	.00	.12	.05	-.18	-.10	.28	.09	.912	.974
I am restless.	.13	.03	.13	.03	-.12	-.02	.38	.08	.667	.549
I am tired.	.03	-.01	.13	.03	-.21	-.06	.26	.04	.959	.912
I feel guilty.	-.06	.00	.13	.03	-.29	-.05	.18	.05	.911	.999
I am doing things at my normal pace.	-.12	.06	.12	.03	-.35	.01	.11	.11	.669	.165
I feel worthless.	-.03	-.04	.12	.03	-.26	-.10	.20	.01	.959	.348
I feel that I can't make decisions.	-.08	.05	.13	.02	-.32	.00	.15	.09	.828	.305
I can't concentrate.	-.05	.08	.13	.02	-.29	.03	.18	.13	.914	.020
I feel hopeless.	-.07	-.05	.12	.03	-.30	-.10	.16	.00	.872	.274
How's your day?	-.08	-.03	.17	.06	-.40	-.15	.23	.09	.901	.901
How would you rate your overall physical health today?	.06	.08	.21	.06	-.32	-.05	.44	.19	.945	.509

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Table 6.9 *Associations between mean heart rate variability measured 120 minutes before rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.18	.00	.13	.02	-.41	-.05	.05	.04	.463	.960
I feel sad.	-.11	.00	.13	.02	-.35	-.04	.13	.05	.736	.960
I feel irritable.	.16	-.02	.12	.02	-.06	-.07	.38	.03	.485	.764
I enjoy what I am doing.	.02	.01	.13	.02	-.22	-.04	.26	.06	.960	.918
I don't care about anything.	-.07	.00	.14	.02	-.33	-.05	.18	.04	.884	.960
I have no appetite during the day.	.14	-.02	.22	.05	-.25	-.11	.54	.07	.835	.912
I worry about sleeping.	-.08	.00	.21	.05	-.46	-.11	.29	.10	.918	.974
I didn't have enough sleep last night.	.07	-.02	.13	.05	-.16	-.12	.31	.07	.884	.901
I am restless.	.13	.01	.14	.02	-.12	-.03	.39	.06	.671	.866
I am tired.	.03	-.01	.13	.02	-.21	-.06	.28	.04	.950	.901
I feel guilty.	-.06	.00	.13	.02	-.31	-.05	.18	.04	.901	.960
I am doing things at my normal pace.	-.13	.04	.13	.03	-.37	-.01	.10	.09	.636	.382
I feel worthless.	-.02	-.04	.13	.03	-.26	-.09	.22	.02	.960	.471
I feel that I can't make decisions.	-.08	.06	.13	.02	-.32	.01	.16	.10	.846	.132
I can't concentrate.	-.04	.07	.13	.02	-.29	.02	.20	.11	.922	.041
I feel hopeless.	-.06	-.05	.13	.02	-.30	-.10	.17	.00	.901	.196
How's your day?	-.04	.00	.18	.05	-.38	-.11	.29	.10	.959	.979
How would you rate your overall physical health today?	.11	.09	.23	.05	-.29	-.01	.52	.19	.901	.326

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Table 6.10 *Associations between mean heart rate variability measured 30 minutes after rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.19	.02	.12	.03	-.41	-.04	.03	.07	.390	.861
I feel sad.	-.12	.01	.12	.03	-.35	-.04	.10	.06	.660	.918
I feel irritable.	.17	-.01	.11	.03	-.04	-.06	.39	.04	.423	.912
I enjoy what I am doing.	-.01	.02	.12	.03	-.24	-.03	.22	.07	.974	.731
I don't care about anything.	-.09	-.01	.13	.03	-.32	-.06	.15	.04	.828	.922
I have no appetite during the day.	.06	-.06	.21	.06	-.32	-.18	.44	.05	.934	.636
I worry about sleeping.	-.11	-.02	.19	.06	-.45	-.15	.24	.10	.884	.918
I didn't have enough sleep last night.	.02	-.05	.13	.06	-.22	-.17	.26	.07	.960	.755
I am restless.	.14	.04	.13	.03	-.10	-.01	.39	.09	.611	.423
I am tired.	.05	.01	.12	.03	-.19	-.04	.28	.06	.918	.911
I feel guilty.	-.06	-.02	.13	.03	-.29	-.07	.17	.03	.911	.784
I am doing things at my normal pace.	-.14	.04	.12	.03	-.36	-.01	.08	.10	.580	.382
I feel worthless.	-.02	-.05	.12	.03	-.25	-.10	.20	.01	.960	.333
I feel that I can't make decisions.	-.06	.04	.12	.03	-.29	-.01	.17	.09	.901	.416
I can't concentrate.	-.02	.06	.12	.02	-.25	.01	.21	.11	.960	.132
I feel hopeless.	-.06	-.05	.12	.03	-.28	-.10	.17	.00	.911	.298
How's your day?	-.13	-.04	.17	.06	-.44	-.16	.18	.09	.782	.872
How would you rate your overall physical health today?	-.01	.05	.21	.06	-.38	-.08	.36	.16	.974	.784

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Table 6.11 *Associations between mean heart rate variability measured 60 minutes after rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.22	.02	.12	.03	-.45	-.03	.01	.07	.328	.784
I feel sad.	-.14	.01	.13	.03	-.38	-.04	.09	.06	.580	.918
I feel irritable.	.16	.00	.12	.03	-.06	-.05	.38	.05	.473	.998
I enjoy what I am doing.	-.01	.02	.13	.03	-.25	-.03	.22	.07	.967	.684
I don't care about anything.	-.11	.00	.13	.02	-.35	-.05	.14	.04	.766	.960
I have no appetite during the day.	.07	-.05	.21	.06	-.32	-.17	.46	.07	.918	.722
I worry about sleeping.	-.13	-.02	.20	.07	-.49	-.15	.22	.10	.835	.922
I didn't have enough sleep last night.	.05	-.02	.13	.06	-.19	-.13	.29	.09	.912	.918
I am restless.	.12	.03	.14	.02	-.13	-.02	.37	.08	.719	.493
I am tired.	.04	.03	.13	.03	-.20	-.02	.28	.08	.924	.473
I feel guilty.	-.04	-.02	.13	.03	-.29	-.07	.19	.03	.918	.715
I am doing things at my normal pace.	-.17	.06	.12	.03	-.40	.01	.05	.11	.463	.178
I feel worthless.	-.04	-.04	.13	.03	-.27	-.09	.19	.02	.926	.471
I feel that I can't make decisions.	-.09	.06	.13	.02	-.32	.01	.15	.11	.828	.121
I can't concentrate.	-.04	.08	.13	.02	-.28	.03	.20	.13	.933	.020
I feel hopeless.	-.07	-.04	.13	.03	-.30	-.09	.17	.01	.900	.382
How's your day?	-.13	-.02	.17	.06	-.45	-.14	.19	.11	.784	.922
How would you rate your overall physical health today?	-.01	.07	.21	.06	-.40	-.06	.38	.19	.974	.617

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Table 6.12 *Associations between mean heart rate variability measured 120 minutes after rating MD symptoms and the within- and between-individual differences in MD symptoms in Study 3*

DDI item	*β*		*SE*		*LCI*		*UCI*		*p*	
	b	*w*	*b*	*w*	*b*	*w*	*b*	*w*	*b*	*w*
I feel happy.	-.25	.01	.13	.02	-.50	-.04	.00	.05	.298	.947
I feel sad.	-.18	.00	.14	.02	-.43	-.05	.08	.05	.500	.974
I feel irritable.	.15	.00	.13	.02	-.09	-.05	.39	.05	.567	.990
I enjoy what I am doing.	-.02	.02	.14	.02	-.28	-.02	.23	.07	.960	.692
I don't care about anything.	-.12	.00	.14	.02	-.39	-.05	.14	.04	.736	.974
I have no appetite during the day.	.08	-.06	.22	.06	-.33	-.18	.48	.07	.918	.692
I worry about sleeping.	-.13	-.02	.20	.07	-.50	-.16	.23	.11	.835	.918
I didn't have enough sleep last night.	.03	.01	.14	.05	-.22	-.09	.28	.11	.960	.954
I am restless.	.11	.03	.15	.02	-.17	-.01	.39	.08	.800	.473
I am tired.	.01	.04	.14	.02	-.25	-.01	.28	.08	.973	.393
I feel guilty.	-.04	-.03	.14	.02	-.30	-.07	.22	.02	.936	.567
I am doing things at my normal pace.	-.22	.05	.13	.02	-.46	.00	.03	.09	.382	.268
I feel worthless.	-.06	-.03	.14	.03	-.31	-.08	.20	.02	.912	.473
I feel that I can't make decisions.	-.11	.04	.14	.02	-.37	-.01	.15	.08	.764	.335
I can't concentrate.	-.06	.06	.14	.02	-.32	.01	.20	.10	.912	.098
I feel hopeless.	-.08	-.04	.14	.02	-.34	-.09	.17	.01	.872	.382
How's your day?	-.14	-.01	.18	.07	-.47	-.14	.19	.12	.782	.960
How would you rate your overall physical health today?	-.01	.06	.22	.07	-.41	-.08	.39	.18	.982	.710

Note. *β* = standardized beta of the fixed effect; *SE* = standard error of the fixed effect; *LCL* = 2.5% confidence interval; *UCL* = 97.5% confidence interval; *p* = *p*-value; *b* = between-individual difference; *w* = within-individual difference.

Discussion

Low physical activity levels were associated with both within- and between-individual differences in different MD symptoms. Low heart rate variability was only found to relate to within-individual differences in two items in the DDI. Heterogeneity among MD symptoms could be observed in the overall scarce significant associations in both activity level and heart rate variability as well as in the ranges of standardized betas in some activity levels and heart rate variabilities.

The links between both low activity level and low heart rate variability and MD severity were vaguely in agreement with previous studies (A. H. Kemp et al., 2010; Saeb et al., 2015). Significant influences of activity levels were mostly observed prior to the momentary feelings were rated and many could be traced back to as far as 120 minutes. The influences of heart rate were smaller in scale compared to activity levels and they exclusively happened before the MD symptoms measures. Significant within-individual differences were only found in two DDI items in heart rate variability – unable to concentrate and doing things with one's normal pace. Even though the symptoms were different from the literature, it corresponded with the literature that only a few MD symptoms were significantly related to heart rate variability and this might explain the inconsistent findings in the link between MD and heart rate variability (Borrione et al., 2018). Reduced activity level and heart rate variability may be used as a warning sign or precaution for the possibly upcoming MD symptoms.

Different patterns in within- and between-individual differences across MD symptoms in both activity level and heart rate activity were observed. However, the patterns of standardized betas of the same symptom in between- or within- subject differences and in activity level or heart rate variability measured before or after the momentary ratings were mostly similar. Only significant within-individual differences were seen in heart rate variability. These were consistent with previous research on varied results in within- and between-individual differences and within-individual differences were more sizeable than between-individual differences in depression (Hamaker, 2012; Kanning et al., 2013; Laukka et al., 2018). The different

results found in between- and within-individual differences might denote there might be greater than formerly expected heterogeneity in MD symptoms. The divergent results may raise a potential problem in using between-individual design to study MD and further use the results in wider application such as policy and clinical diagnose and treatments.

Among the DDI items significantly related to activity level, positive mood was the only item that had significant associations in within- and between-individual differences. This confirmed the previous finding on the relationship between positive mood and activity level (Bossmann et al., 2013). While positive affect was significantly predicted by activity level, negative affect was not. The divergent results in positive and negative affects indicated albeit positive affect was different from negative affect, it was not the opposite of negative affect. This was in line with the literature (Cacioppo & Berntson, 1999; Danhauer et al., 2013; Watson, Clark, & Carey, 1988; Watson, Clark, & Tellegen, 1988). Only positive affect was associated with activity level might also imply increasing activity level had no effect on negative affect. Therefore, if having negative affect was the primary symptoms in MD patients, other approaches would be required to diminish negative affect.

Limitations and future directions

There was less heart rate variability data than the activity level data. No heart rate variability data were collected in 18 female participants. The positions of the devices may be a possible cause. Some participants felt uncomfortable wearing the activity sensor. This may result from the long hours participants were required to wear the sensor in a sampling day and the length of the study being 14 days. Using devices that are easier and more comfortable to wear for a prolonged period may be more ideal for future studies. However, considering the variety of devices on offer in the market, researchers may want to include other issues such as sensitivity, precision, data computing time, and power efficiency in evaluation (Kirchner et al., 2018).

Within-individual differences do provide new perspective because within-individual analyses might yield results different from between-individual analyses (A.

J. Fisher et al., 2018; Hamaker, 2012; P. C. M. Molenaar, 2004). The within-individual variances might be four times larger than between-individual variances (A. J. Fisher et al., 2018). Future studies could include this in the study design, and this may yield unforeseen results to further our knowledge of MD. Future studies could investigate the precise time frame of the influences of activity level and heart rate variability starting to affect MD symptoms. These changes could be used as an alarm to notify MD patients and hopefully to prevent MD symptoms or episodes from kicking in.

Next chapter will discuss whether network theory could be used to explain MD and potential issues related to the network theory.

Chapter 7 Temporal relationships among depressive symptoms

Introduction

Depression: a unitary entity or a cluster of interconnected constituents

The classification system of mental disorders described the disorders using symptoms, which formed the diagnostic criteria. This unitary model ("one diagnosis, one disease process") was the mainstream view of psychiatric disorders and greatly influenced relevant academic and pharmacological research in psychiatry. However, there are also views about whether such an entity is discrete or categorical – a person either has depression or not – or continuously distributed across all individuals from very-low levels (characteristic of a non-pathological state) to very-high (attracting clinical attention). Both views would fit in what Kendler, Zachar, and Craver (2011) referred to as essentialist kinds: each disorder has a specific set of etiological factors that are qualitatively invariant across people. Essentialist kinds may well explain infectious diseases. But they are ill-suited in depicting biological phenomena, chronic diseases, and psychiatric disorders because multiple environmental, genetic, metabolic, behavioral factors are involved. These may interact with each other and contribute variously to the observed disease, disorder, or biological phenomena. Moreover, essentialist kinds cannot fully capture the heterogeneous feature of psychiatric disorders. For example, this can be observed in the literature where some studies showed the same (Bhar et al., 2008) while some studies reported different patterns (Fournier et al., 2013) of changes in different depressive symptoms in patients who were under clinical treatments; differential variations of patterns among the symptoms is a central question of this thesis.

Also, Reiger et al. (2013) field tested the reliability (agreement between diagnosis) of several psychiatric disorder diagnoses listed in the Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V) in 11 medical centers in the U.S. and Canada. Depending on the interclass kappa values, the diagnostic reliability can

fall into a range of very good (kappa = .6–.79), good (kappa = .4–.59), questionable (kappa = .2–.39), and unacceptable (kappa < .2). The DSM-V diagnosis of major depression (MD) fell into a questionable range in this field trial – in adults, the diagnostic reliability was good, questionable, and unacceptable in one, two, and one medical centers, respectively; in children, the diagnostic reliability was questionable in two medical centers. Their results demonstrated the pressing need to review the classification and diagnostic criteria of psychiatric disorders. Relevantly for this research, this reliability may explain etiological heterogeneity in psychiatric disorders because different doctors or diagnostic instruments may focus on different symptoms and thereby either detect or did not detect the disorder in their patients.

Network theory

Kendler et al. (2011) proposed an alternative conceptualization of psychiatric disorders that they termed mechanistic property clusters (MPC). This concept was firstly mentioned in Kendler (2008) as a mechanistic approach, where he described psychiatric disorders were caused by multi-level causal loops and interactions. In the MPC view, there is no single underlying entity that causes the coalescence of groups of symptoms (disorders). Instead, symptoms coalescence and are sustained via mutually reinforcing associations among themselves. The MPC conceptualization of disorders may better deal with phenomena that the essentialist view struggles to account for. These include ubiquitous co-morbidity (co-existence of multiple disorders) and clinical heterogeneity (patients thought to have the same disorder varying in specific symptoms) (Borsboom & Cramer, 2013; Borsboom et al., 2011; Cramer et al., 2010). The former is because the symptoms may reinforce each other across putative disorders: the symptoms thought to be caused by different disorders according to the traditional view may overlap or they are causally connected. The latter is because the patterns of causal associations among symptoms may differ across individuals (contributing to heterogeneous sets of symptoms). A similar idea of symptoms forming a causal network, where the presence of current psychiatric symptoms was caused by the same and/or other

earlier psychiatric symptoms, was advocated by Borsboom (2008) and summarized as the network theory (Borsboom, 2017). In the network theory, psychiatry symptoms are presumed to have causal relationships between each other (Borsboom, 2017). These interconnected symptoms form a network of symptoms and they collectively represent a psychiatric disorder. It has been applied in explaining several mental disorders including MD (Cramer et al., 2016; Fried, Epskamp, et al., 2016).

The network theory could explain the structure, comorbidity, and dynamics of mental disorders. Borsboom (2017) adopted an interventionist theory of causation to explain the causal relationships between symptoms (Woodward, 2005). This theory describes when a causal relationship exists between two symptoms, the expression of one symptom would be altered by interventions or treatments of another symptom. Each symptom is illustrated by a node in a network (Borsboom, 2017). Connections between nodes are nodes, which depict direct causal relationships among symptoms. Causation may be unidirectional or bidirectional. Strong causal relationships between the nodes in a network generate feedback loops and maintain the existing causal relationships. Networks could be influenced by both internal and external factors – changes in nodes within the network and factors outside of the network (excluding the nodes). These may include all psychological and biological causes in an individual and causes from the environments surrounding the individual. Depending on the strength of connections between particular nodes, network structures may be synchronized when the connections are strong (the activation of one symptom is very likely to activate most other symptoms in the network) or clustered when the connections are weak (one activated symptom only activates certain symptoms and other symptoms remain inactive).

Comorbidity between psychiatric disorders could be explained by the network theory, too. Comorbidity arises when two or more networks share bridge symptoms – symptoms that connect separate networks. The level of connectivity between nodes within a network differ from pair to pair. Therefore, network theory

could be readily applied to explain the dynamics of psychopathology. In strongly connected networks, transition from an inactivated state to an activated state may result in hysteresis – a self-sustaining activated state even after the triggers are removed (Cramer, 2013; Cramer et al., 2016). When weakly connected networks are activated, the activated state is less likely to last and the network would return to the inactivated state. "Mental disorders then arise when groups of tightly coupled symptoms actively maintain each other, leading to a cluster of psychopathology symptoms that becomes self-sustaining" (Borsboom, 2017, p. 7). A simulation study on MD reported the amount of stress had to be removed from a system is more than the amount of stress required to induce state transition initially (Cramer et al., 2016). Applying network theory to study how disorders arise in healthy people, it could indicate early signs of possible transition into a disordered state (Fried et al., 2017).

An important property of any network is the centrality of its nodes. Centrality of symptoms shows the relative importance of symptoms (Opsahl, Agneessens, & Skvoretz, 2010; Sciarra, Chiarotti, Laio, & Ridolfi, 2018) within a network, which could be used in identifying key symptoms in treatment plans. But there are different centrality measures and they reveal different aspects of the topography of nodes in a network. Centrality measures including instrength (how much a node could be predicted by other nodes in the network), outstrength (how much a node could predict other nodes), betweenness (the shortest path of a node between two other nodes), and closeness (the shortest path to all other nodes in a network) (A. J. Fisher et al., 2017; Fornito et al., 2016; Opsahl et al., 2010).

Although the network theory provides a new lens into psychiatric disorders, it is not without limitations and there had been some debates. The most critical question is: how to empirically test this, in comparison to depression-as-unitary-entity view? Three independent networks – temporal, contemporaneous, and between-subjects networks – were used to test the relationships between MD symptoms and the structure of MD (Epskamp, Waldorp, et al., 2018). Temporal networks reveal lagged relationships, where the value of a variable measured at a

time point predicts the values of the same (self- loop) or the other variables in the network assessed at the subsequent time point. These temporal relationships might explain the causal relationships between variables because one of the premises of causality is causes proceed effects; the autoregressive paths capture the changes in the variables themselves, including variance due to their underlying but time-varying common cause, whereas the cross-lagged paths capture potentially causal associations between variables, conditional on autoregressive paths. Vector auto-regression (VAR) is widely used to study causality and forecasting in economics (Coad, 2010; Jangili, 2011; Stock & Watson, 2001; Taghavi, 2001). An edge in temporal networks is obtained by controlling for all other variables in the previous sampling time in a regression model (Epskamp, Waldorp, et al., 2018). VAR has been used in nursing studies on the causality between several vital signs and cardiorespiratory instability, too (Bose et al., 2017). In a small sample of time-series data, VAR was reported as a suitable tool to study causality between MD and physical activity (Rosmalen et al., 2012). Temporal networks could catch the time-lagged relationships between some variables. There are also possibilities where temporal associations might not infer causality such as "a unidimensional auto-correlated factor model would lead to every variable predicting every other variable over time" (Epskamp, van Borkulo, et al., 2018, p. 417). In addition, successfully constructing temporal networks is limited by sufficient statistical power of data and the lag interval recorded – data recorded every few hours cannot advise temporal relationships occurred over a few seconds.

However, the associations between other variables may happen instantaneously and these associations could not be captured by temporal networks but they may be explained by contemporaneous networks. Contemporaneous networks could inform the structure of a network but they do not provide information on the relationships between variables in networks (A. J. Fisher et al., 2017). Contemporaneous networks describe partial directed correlations between variables at the same time after controlling for all temporal effects and the linear

effects of other variables at the same time (Epskamp, van Borkulo, et al., 2018; Epskamp, Waldorp, et al., 2018; Wild et al., 2010).

Both temporal and contemporaneous networks are within-subjects networks in that they describe co-variation within individuals. The more frequent the assessment the better the estimation of these two networks and the estimation of between-subjects networks improves with the number of participants. For example, an association in the former means that when an individual was more worried than his/her usual at time one he/she would feel more tired than his/her usual at time two, controlling for all other autoregressive and cross-lagged associations. An association in the latter, in contrast, could mean that while an individual is more tired than his/her usual he/she would concurrently have more concentration problems, regardless of his/her levels of tiredness, concentration problems and all other symptoms at the previous time-point. The differences between subjects could be observed in between-subject networks, which could show, for example, that the more worried people are generally, the less tired they feel, even if there is a positive association between these symptoms within individuals over time.

Moreover, Forbes, Wright, Markon, and Krueger (2017) argued the networks were unstable due to measurement errors. As a result, the results may need to be examined with standards higher than the normal ones to reach sound conclusions. Along the same line of argument, Steinley, Hoffman, Brusco, and Sher (2017) tested the network theory and found most of the results were not different from the results obtained by chance. The issue on multiple testing was highlighted, too. They then argued the network results were highly nonreplicable and eying on the recent replication crisis movement in science including Psychology, those who want to apply the relevant findings should be more cautious (V. E. Johnson et al., 2017). Later, Borsboom et al. (2017) reanalyzed the data Forbes et al. (2017) used and claimed the networks were more replicable than these authors claimed. Forbes, Wright, Markon, and Krueger (2017) also reanalyzed the data and tested replicability of the networks by randomly splitting the data into 10 datasets. They

concluded the replicability of network analysis are limited in within and between subjects. There are other statistical issues of network theory including lacking appropriate methods in handing ordinal data and potential flaws in the current method in treating missing data (Epskamp, 2017).

The above arguments regarding the pitfalls and limitations of network theory showed the network theory is still in its early stage of development and these are common and healthy processes in the development of new theories. Also, the theory is drawing more attentions in the field. This chapter sought to address the two issues mentioned above – essentialist view vs. network theory and the stability of networks by conducting three time-series studies and analyzing the lagged relationships between MD symptoms, the level of connectivity of MD symptoms, and the replicability across the studies. A potential issue of multiple comparison was addressed by using false discovery rate to adjust all *p*-values. Moreover, significance level of .001 rather than the conventional .05 was employed to get solid conclusions.

The studies

One way to test these competing views of the nature of MD is to collect time-series data of depression symptoms and study the associations among the symptoms over time. Levels of depression symptoms vary over time – hours, days, weeks, or months. This may be caused by changes in an underlying latent entity (MD) (a prediction derived from the essentialist view) or by the up or down regulations between the symptoms (a prediction from the MPC view and the network theory). These two explanations are not mutually exclusive and they may coexist (Epskamp, Rhemtulla, & Borsboom, 2017). If the former is the case, associations between symptoms *across* time should reduce to non-significant levels once general changes (captured by autoregressive path among the symptoms) in their shared variance are controlled for. However, if there are associations among symptoms over time – e.g., fatigue at time one correlates with concentration difficulties at time two over and above the general (shared) fluctuations in symptoms, the network theory is supported. In other words, if the essentialist view

holds, there is no reason to expect cross-lagged associations among symptoms once the autoregressive trajectories of these symptoms are controlled for (H16). But no matter which explanation the results support, it does not dismiss the other explanation. Contemporaneous network and between-subject network are used to explore the associations not captured by temporal network and the structure of MD. Two centrality measure – instrength and outstrength – are used to test the predictabilities of MD symptoms in the three networks (A. J. Fisher et al., 2017). There being systematic variability among symptoms in their centrality, especially in temporal networks, would be consistent with the network view because there is no reason for one symptom to be more central than others according to the entity-view: this view sees all symptoms merely as indicators or the single underlying processes. Other than testing the networks in the three studies separately, the stability of the networks is tested by analyzing the replicability of the networks. If the networks do replicate, this shows they are stable and H16 gains substantial support.

Materials and Method

The participant, material, and procedures used here were the same as those described in materials and method in Studies 1, 2, and 3 in Chapters 2–6.

Results

All analyses were conducted in RStudio version 1.1.463. The Gaussian Graphic Model (GGM) was used to conduct network analysis in RStudio as implemented in the R package *mlVAR,* version 0.4.1 (Epskamp, Waldorp, et al., 2018). Univariate multilevel regression models, which calculate within-subject variances, were used in temporal and contemporaneous networks to estimate parameters for each individual. To simplify the models, correlated random effects excluding those appeared in the same models were used in both temporal and contemporaneous networks, meaning that within-subject (co-)variances were accounted for as well as between-subject differences in these networks. Between-

subjects networks use the estimations of sample-means of each participant on all variables. In the three studies, variables only measured once a day were removed from analysis because the two-step multilevel VAR only calculates measurements at time t and their subsequent measurements at time t+1. These variables were reduced to NAs as per listwise deletion. Therefore, associations between variables measured on different days were not analyzed (e.g., over-night cross-lagged or autoregressive paths). The effect sizes of the networks are standardized betas from multi-level models for the temporal networks, partial correlation coefficients among the residuals of the variables from multi-level models for the contemporaneous networks, and partial correlation coefficients between intercepts from the multi-level models for the between-subject networks. All temporal connections including the significant and non-significant ones between symptoms in Studies 1, 2, and 3 were shown in Figures 7.1–7.3, respectively. Blue arrows illustrate positive connections while red arrows denote negative connections. To address the issue of multiple comparison, all *p*-values were corrected using false discovery rate. The centrality of the temporal networks was analyzed by using matrices of betas while partial correlation coefficients were used to calculate the centrality of the contemporaneous and between-subject networks.

To test the stability of the networks, the replicability of the three studies was also tested by comparing the effect sizes of the networks (e.g., standardized betas) with Spearman's rank-order correlation. If the temporal networks were stable across three studies, the support for either the essentialist or the network view would be even more robust. Meta-analysis of the networks was also conducted to see whether there were shared patterns across studies. The DDI items only used in one of the studies were removed from meta-analysis.

Study 1

The time-series data of 6,392 data points collected from 127 participants were analyzed. The DDI items only measured once a day were removed from analysis. These items were "*I have no appetite during the day*", "*I worry about*

sleeping", "*I feel that I didn't have enough sleep last night*", and "*How's your day*". Almost all symptoms measured at time t significantly predicted the ratings of the same symptom at time t+1 with one exception of feeling irritable (β = .09, p = .011). Scattered significant temporal associations were observed between the DDI items (Figure 7.1; Table 7.1). As for temporal, cross-lagged associations, greater concentration at t was associated with feeling able to get things done at t+1 (β = .10, p < .001). Participants who felt more worthless at time t felt less hopeful at time t-1 (β = .13, p < .001). These few significant temporal associations provided some support for the network theory; but only 12 of the 121 possible associations were significant, so the evidence was weak.

The importance of MD symptoms in the temporal network could be seen in centrality measures. The outstrength ranking revealed feeling sad and worthless were the symptoms that predicted the most symptoms while the instrength ranking showed feeling hopeless and unable to concentrate were the symptoms that mostly affected by other symptoms (Table 7.2). In the temporal network, some symptoms connected with more symptoms than others and the symptoms have high level of connectivity might be more important than others. This supported the network theory and challenged the essentialist view because according to the essentialist view, MD symptoms would not differ in centrality in temporal networks.

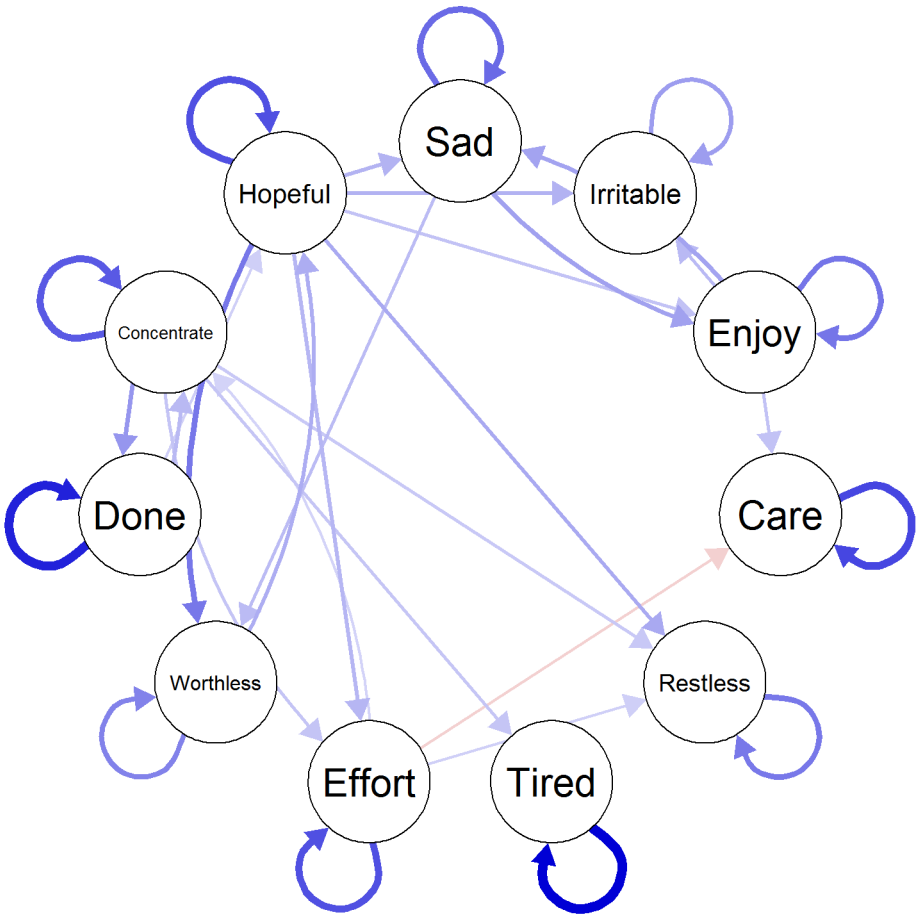


Figure 7.1 Temporal network in Study 1

Table 7.1 *Standardized betas, standard errors, and p-values of the temporal network in Study 1*

From	To	*β*	*SE*	*p*
Sad	Sad	.14	.03	< .001
Sad	Irritable	.05	.03	.225
Sad	Enjoy	.09	.03	.037
Sad	Care	.00	.03	.972
Sad	Restless	-.01	.03	.780
Sad	Tired	.03	.03	.534
Sad	Effort	.00	.02	.926
Sad	Worthless	.06	.03	.052
Sad	Done	.00	.03	.974
Sad	Concentrate	.01	.03	.789
Sad	Hopeless	.02	.03	.616
Irritable	Sad	.05	.03	.179
Irritable	Irritable	.09	.03	.011

From	To	*β*	*SE*	*p*
Irritable	Enjoy	.03	.03	.386
Irritable	Care	-.01	.02	.833
Irritable	Restless	.01	.03	.923
Irritable	Tired	-.03	.03	.544
Irritable	Effort	.01	.02	.837
Irritable	Worthless	-.01	.02	.890
Irritable	Done	.00	.03	.951
Irritable	Concentrate	-.01	.03	.881
Irritable	Hopeless	.02	.02	.531
Enjoy	Sad	.09	.03	.006
Enjoy	Irritable	.06	.02	.025
Enjoy	Enjoy	.13	.03	< .001
Enjoy	Care	.06	.02	.070
Enjoy	Restless	.00	.02	1.000
Enjoy	Tired	.00	.02	.973
Enjoy	Effort	.01	.02	.782
Enjoy	Worthless	.03	.02	.477
Enjoy	Done	-.02	.03	.602
Enjoy	Concentrate	.03	.02	.363
Enjoy	Hopeless	.01	.03	.824
Care	Sad	.04	.02	.157
Care	Irritable	.02	.02	.653
Care	Enjoy	.01	.02	.739
Care	Care	.17	.03	< .001
Care	Restless	.00	.02	.934
Care	Tired	-.02	.02	.516
Care	Effort	-.01	.02	.802
Care	Worthless	.00	.02	.974
Care	Done	.01	.02	.731
Care	Concentrate	-.01	.02	.780
Care	Hopeless	.01	.02	.742
Restless	Sad	.01	.02	.874
Restless	Irritable	-.01	.02	.837
Restless	Enjoy	.02	.02	.422
Restless	Care	.01	.02	.819
Restless	Restless	.12	.02	< .001
Restless	Tired	.03	.02	.291
Restless	Effort	.02	.02	.449
Restless	Worthless	.01	.02	.715
Restless	Done	.00	.02	.949
Restless	Concentrate	.03	.02	.290
Restless	Hopeless	.01	.02	.780
Tired	Sad	.01	.02	.723
Tired	Irritable	.00	.02	.981

From	To	*β*	*SE*	*p*
Tired	Enjoy	.00	.02	1.000
Tired	Care	.01	.02	.731
Tired	Restless	.00	.02	.998
Tired	Tired	.24	.02	< .001
Tired	Effort	.02	.02	.581
Tired	Worthless	-.02	.02	.402
Tired	Done	.01	.02	.679
Tired	Concentrate	.00	.02	.970
Tired	Hopeless	.00	.02	.926
Effort	Sad	-.01	.02	.679
Effort	Irritable	-.01	.02	.744
Effort	Enjoy	.02	.02	.547
Effort	Care	-.04	.02	.091
Effort	Restless	.04	.02	.116
Effort	Tired	.03	.02	.379
Effort	Effort	.16	.02	< .001
Effort	Worthless	-.02	.02	.498
Effort	Done	.01	.02	.692
Effort	Concentrate	.04	.02	.134
Effort	Hopeless	.01	.02	.669
Worthless	Sad	.01	.03	.919
Worthless	Irritable	.01	.03	.926
Worthless	Enjoy	.01	.03	.793
Worthless	Care	.04	.03	.272
Worthless	Restless	.01	.03	.784
Worthless	Tired	.04	.03	.404
Worthless	Effort	.00	.03	.974
Worthless	Worthless	.12	.03	< .001
Worthless	Done	.01	.02	.733
Worthless	Concentrate	.03	.02	.398
Worthless	Hopeless	.08	.03	.011
Done	Sad	-.02	.02	.535
Done	Irritable	.02	.02	.471
Done	Enjoy	.03	.02	.454
Done	Care	.03	.02	.215
Done	Restless	-.03	.02	.338
Done	Tired	-.01	.02	.808
Done	Effort	.02	.02	.593
Done	Worthless	.01	.02	.784
Done	Done	.21	.02	< .001
Done	Concentrate	.07	.02	.006
Done	Hopeless	.05	.02	.076
Concentrate	Sad	.02	.02	.689
Concentrate	Irritable	.03	.02	.378

From	To	*β*	*SE*	*p*
Concentrate	Enjoy	.02	.02	.642
Concentrate	Care	.01	.02	.782
Concentrate	Restless	.05	.02	.091
Concentrate	Tired	.05	.02	.070
Concentrate	Effort	.05	.02	.029
Concentrate	Worthless	.02	.02	.517
Concentrate	Done	.10	.02	< .001
Concentrate	Concentrate	.15	.02	< .001
Concentrate	Hopeless	.02	.02	.640
Hopeless	Sad	.07	.03	.070
Hopeless	Irritable	.07	.03	.041
Hopeless	Enjoy	.06	.03	.146
Hopeless	Care	.02	.03	.731
Hopeless	Restless	.08	.03	.011
Hopeless	Tired	-.02	.03	.699
Hopeless	Effort	.07	.02	.016
Hopeless	Worthless	.13	.03	< .001
Hopeless	Done	.01	.03	.767
Hopeless	Concentrate	.02	.02	.556
Hopeless	Hopeless	.16	.03	< .001

Note. *β* = standardized beta; *SE* = standard error; *p* = *p*-value.

Table 7.2 *Outstrength and instrength of the symptoms in the temporal network in Study 1*

Outstrength		Instrength	
DDI item	*z*	DDI Item	*z*
Sad	.32	Hopeless	.54
Worthless	.30	Concentrate	.37
Enjoy	.29	Enjoy	.31
Irritable	.29	Done	.29
Tired	.25	Sad	.29
Concentrate	.25	Effort	.24
Restless	.24	Worthless	.23
Care	.23	Irritable	.17
Hopeless	.23	Care	.14
Effort	.21	Restless	.14
Done	.19	Tired	.08

Note. z = z-score

Feeling hopeless was the most influential symptom in the contemporaneous network. It significantly ($p < .001$) associated with eight symptoms – feeling sad ($pr = .15$), feeling irritable ($pr = .09$), not enjoying what one was doing ($pr = .10$), not caring what one was doing ($pr = .05$), feeling restless ($pr = .07$), feeling worthless ($pr = .25$), unable to get things done ($pr = .11$), and unable to concentrate ($pr = .11$) (Table D.1 in Appendix D). Doing things effortfully was the second most influential symptom and it significantly related to five symptoms. Feeling sad, feeling irritable, not enjoying what one was doing significantly related to four symptom and they were the third most influential symptoms. Feeling restless and feeling tired were the least influential symptoms. The number of significant contemporaneous associations indicated the structure of MD is rather versatile and some symptoms related to others concurrently. For centrality, feeling irritable and enjoying what one was doing were the symptoms connected with the most symptoms in instrength and outstrength (Table 7.3). Although these findings *per se* did not support or reject the essentialist view or the network theory, it weakened the claim of the essentialist view, where the relationships between symptoms are not addressed.

Table 7.3 *Outstrength and instrength of the symptoms in the contemporaneous and between-subjects network in Study 1*

Contemporaneous network		Between-subjects network	
Outstrength and Instrength		Outstrength and Instrength	
DDI item	*z*	DDI Item	*z*
Irritable	1.05	Sad	1.92
Enjoy	1.01	Concentrate	1.80
Sad	.96	Hopeless	1.75
Hopeless	.95	Done	1.61
Concentrate	.86	Enjoy	1.51
Done	.80	Worthless	1.43
Worthless	.66	Irritable	1.25
Effort	.64	Tired	1.18
Care	.56	Restless	1.12
Tired	.55	Care	1.05
Restless	.47	Effort	.76

Note. z = z-score

In the between-subject network, feeling sad, not enjoying what one was doing, and unable to concentrate were significantly related to two symptoms (Table D.2 in Appendix D). Four symptoms significantly associated with one symptom – feeling irritable, feeling worthless, unable to get things done, and feeling hopeless. There were four symptoms did not significantly correlate with any symptoms – caring about nothing, feeling restless, feeling tired, and doing things effortfully. The symptoms that predicted the most symptoms and were predicted by most symptoms were feeling sad and unable to concentrate (Table 7.3).

Different associations observed in the three networks revealed the complicated structure of MD and the intertwined relationships between MD symptoms. To test the results of Study 1, two more studies were conducted.

Study 2

A total number of 3,955 data points from 78 participants were collected. The following items were removed from analysis because they were only measured once per day "*I have no appetite during the day*", "*I worry about sleeping*", "*I feel that I didn't have enough sleep last night*", "*How's your day*" and "*How would you rate your overall physical health today*". Except feeling sad (β = .12, p = .006) and not enjoying what one was doing (β = .11, p = .006), feeling more of a symptom significantly predicted the subsequent enhanced feeling of the same symptom (Figure 7.2; Table 7.4). Feeling less hopeful at time t was predicted by feeling more worthless at time t-1 (β = .12, p < .001). Reduced concentration at time t was linked to feeling unable to get things do at time t+1 (β = .16, p < .001). The number of significant associations among MD symptoms was similar to that in Study 1 and among the 144 possible associations, 12 were significant but 10 of these were auto-correlations. The network theory was vaguely supported.

Outstrength and instrength were analyzed to test the importance of MD symptoms in the temporal network. Feeling sad and unable to get things done predicted the most symptoms while unable to concentrate and feeling worthless were predicted by the most symptoms (Table 7.5). MD symptoms bearing varied

level of importance in the temporal network as indicated by centrality attenuated the essentialist view because based on the essentialist view, symptoms would not have different levels of centrality.

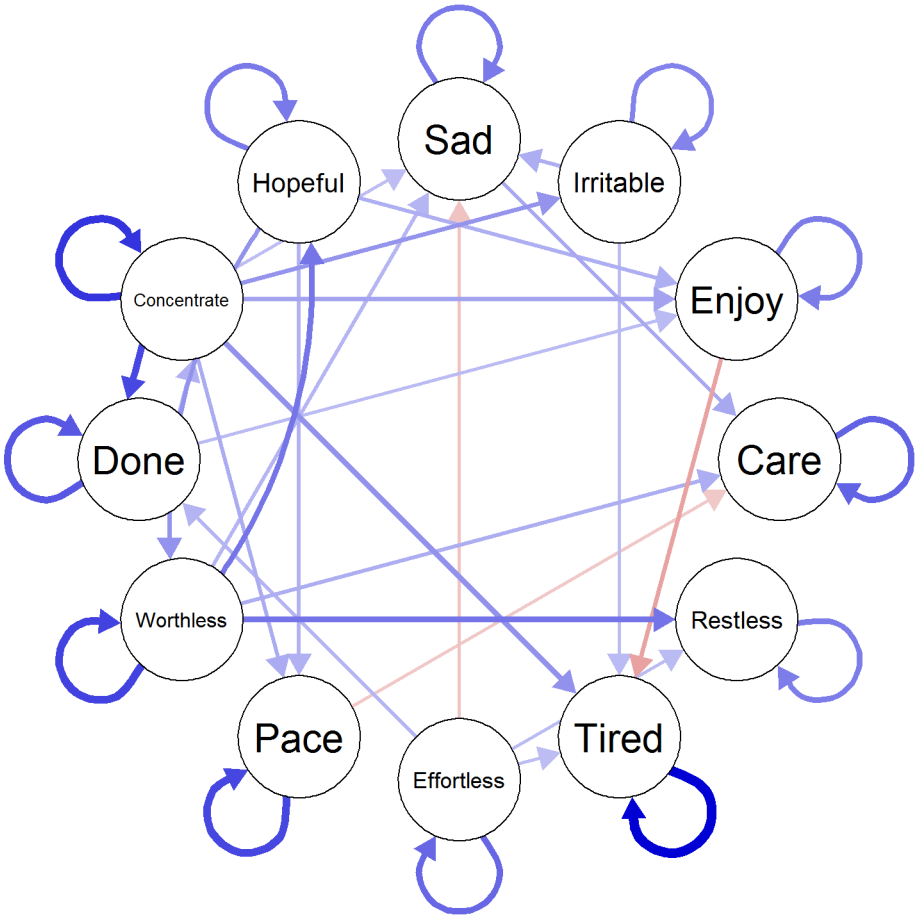


Figure 7.2 Temporal network in Study 2

Table 7.4 *Standardized betas, standard errors, and p-values of the temporal network in Study 2*

From	To	*β*	*SE*	*p*
Sad	Sad	.12	.03	.006
Sad	Irritable	.04	.03	.327
Sad	Enjoy	.01	.03	.926
Sad	Care	.08	.04	.107
Sad	Restless	.01	.03	.902
Sad	Tired	.00	.03	.987
Sad	Effortless	-.05	.03	.298
Sad	Pace	-.03	.03	.638
Sad	Worthless	.00	.02	.987

From	To	*β*	*SE*	*p*
Sad	Done	.04	.03	.340
Sad	Concentrate	.04	.03	.333
Sad	Hopeless	.02	.02	.546
Irritable	Sad	.07	.03	.076
Irritable	Irritable	.11	.03	< .001
Irritable	Enjoy	-.01	.03	.891
Irritable	Care	.01	.03	.886
Irritable	Restless	.03	.03	.465
Irritable	Tired	.06	.03	.115
Irritable	Effortless	.04	.03	.324
Irritable	Pace	-.04	.03	.431
Irritable	Worthless	.03	.02	.417
Irritable	Done	-.02	.03	.730
Irritable	Concentrate	-.02	.03	.732
Irritable	Hopeless	.03	.03	.416
Enjoy	Sad	.05	.03	.240
Enjoy	Irritable	.00	.03	1.000
Enjoy	Enjoy	.11	.04	.006
Enjoy	Care	-.04	.03	.311
Enjoy	Restless	-.02	.02	.549
Enjoy	Tired	-.08	.03	.006
Enjoy	Effortless	.02	.03	.698
Enjoy	Pace	.02	.03	.768
Enjoy	Worthless	-.01	.03	.858
Enjoy	Done	-.05	.03	.211
Enjoy	Concentrate	-.03	.03	.506
Enjoy	Hopeless	.01	.02	.777
Care	Sad	-.01	.03	.854
Care	Irritable	-.02	.03	.675
Care	Enjoy	-.03	.03	.590
Care	Care	.14	.03	< .001
Care	Restless	-.05	.03	.363
Care	Tired	-.03	.03	.518
Care	Effortless	-.02	.03	.692
Care	Pace	-.03	.03	.455
Care	Worthless	-.01	.02	.733
Care	Done	.04	.03	.363
Care	Concentrate	.04	.03	.272
Care	Hopeless	.03	.02	.518
Restless	Sad	-.02	.02	.707
Restless	Irritable	.01	.02	.890
Restless	Enjoy	-.01	.03	.768
Restless	Care	-.01	.02	.768
Restless	Restless	.11	.03	< .001

From	To	*β*	*SE*	*p*
Restless	Tired	.02	.02	.717
Restless	Effortless	.02	.02	.506
Restless	Pace	.04	.02	.272
Restless	Worthless	.01	.02	.666
Restless	Done	-.04	.02	.202
Restless	Concentrate	.01	.03	.806
Restless	Hopeless	.02	.02	.547
Tired	Sad	.03	.02	.460
Tired	Irritable	.02	.02	.513
Tired	Enjoy	.03	.02	.341
Tired	Care	-.02	.02	.517
Tired	Restless	-.02	.02	.642
Tired	Tired	.22	.03	< .001
Tired	Effortless	.01	.02	.840
Tired	Pace	-.01	.02	.865
Tired	Worthless	.00	.02	.932
Tired	Done	.02	.02	.533
Tired	Concentrate	.02	.03	.648
Tired	Hopeless	.01	.02	.746
Effortless	Sad	-.05	.03	.134
Effortless	Irritable	.02	.03	.604
Effortless	Enjoy	.04	.03	.313
Effortless	Care	.03	.02	.426
Effortless	Restless	.06	.03	.116
Effortless	Tired	.06	.03	.085
Effortless	Effortless	.13	.03	< .001
Effortless	Pace	-.03	.03	.604
Effortless	Worthless	.04	.02	.280
Effortless	Done	.07	.03	.059
Effortless	Concentrate	.05	.03	.179
Effortless	Hopeless	.04	.03	.321
Pace	Sad	.01	.03	.764
Pace	Irritable	.00	.02	.997
Pace	Enjoy	.00	.03	.928
Pace	Care	-.05	.02	.094
Pace	Restless	.00	.02	.932
Pace	Tired	.01	.02	.768
Pace	Effortless	.02	.02	.698
Pace	Pace	.16	.02	< .001
Pace	Worthless	.00	.02	.942
Pace	Done	-.01	.02	.879
Pace	Concentrate	.01	.02	.837
Pace	Hopeless	.01	.02	.713
Worthless	Sad	.06	.03	.153

From	To	*β*	*SE*	*p*
Worthless	Irritable	.05	.04	.376
Worthless	Enjoy	.03	.04	.648
Worthless	Care	.07	.03	.126
Worthless	Restless	.12	.04	.020
Worthless	Tired	.02	.04	.714
Worthless	Effortless	.01	.04	.875
Worthless	Pace	.01	.03	.854
Worthless	Worthless	.16	.04	< .001
Worthless	Done	.04	.03	.421
Worthless	Concentrate	.04	.03	.443
Worthless	Hopeless	.12	.03	< .001
Done	Sad	.04	.02	.192
Done	Irritable	.04	.03	.240
Done	Enjoy	.06	.03	.115
Done	Care	.04	.03	.297
Done	Restless	.05	.03	.292
Done	Tired	-.01	.03	.840
Done	Effortless	.04	.03	.340
Done	Pace	-.02	.04	.707
Done	Worthless	.01	.03	.768
Done	Done	.15	.03	< .001
Done	Concentrate	.07	.03	.085
Done	Hopeless	.02	.02	.590
Concentrate	Sad	.06	.03	.134
Concentrate	Irritable	.09	.03	.016
Concentrate	Enjoy	.08	.03	.037
Concentrate	Care	.04	.02	.226
Concentrate	Restless	.04	.03	.343
Concentrate	Tired	.09	.03	.006
Concentrate	Effortless	.05	.03	.257
Concentrate	Pace	.07	.03	.079
Concentrate	Worthless	.01	.02	.805
Concentrate	Done	.16	.04	< .001
Concentrate	Concentrate	.18	.03	< .001
Concentrate	Hopeless	.03	.03	.488
Hopeless	Sad	.02	.03	.688
Hopeless	Irritable	.01	.04	.910
Hopeless	Enjoy	.07	.03	.126
Hopeless	Care	.01	.03	.921
Hopeless	Restless	.02	.04	.733
Hopeless	Tired	.00	.03	.998
Hopeless	Effortless	.01	.03	.820
Hopeless	Pace	.07	.03	.124
Hopeless	Worthless	.09	.03	.020

From	To	*β*	*SE*	*p*
Hopeless	Done	.06	.03	.205
Hopeless	Concentrate	.01	.03	.926
Hopeless	Hopeless	.12	.03	< .001

Note. *β* = standardized beta; *SE* = standard error; *p* = *p*-value.

Table 7.5 *Outstrength and instrength of the nodes in the temporal network in Study 2*

Outstrength		Instrength	
DDI item	*z*	DDI Item	*z*
Done	.54	Concentrate	.73
Sad	.43	Worthless	.58
Restless	.42	Effortless	.48
Care	.39	Done	.40
Tired	.38	Hopeless	.37
Enjoy	.37	Irritable	.35
Pace	.36	Enjoy	.32
Hopeless	.35	Sad	.31
Concentrate	.33	Care	.30
Irritable	.32	Restless	.21
Effortless	.29	Tired	.19
Worthless	.22	Pace	.12

Note. z = z-score

In the contemporaneous network, feeling sad, feeling irritable, and unable to get things done were the most influential symptoms and they had significant connections with four symptoms (Table D.3 in Appendix D). Not enjoying what one was doing, feeling tired, doing things effortfully, and feeling worthless were the second most influential symptoms and they were significantly connected with three symptoms. Feeling restless, unable to concentrate, and feeling hopeless were significantly associated with two symptoms. The least influential symptoms were caring about nothing and not doing things with one's normal pace and they only significantly related to one symptom. Consistent with the contemporaneous network in Study 1, some contemporaneous connections were found, which showed the structure of MD was complex and unstable. Feeling sad and irritable were the top two symptoms affecting and being influenced by the most symptoms (Table 7.6). Certain MD symptoms were more connected than other symptoms,

which tempered the essentialist view because it does not address the relationships between MD symptoms.

Table 7.6 *Outstrength and instrength of the nodes in the contemporaneous and between-subjects networks in Study 2*

Contemporaneous network		Between-subjects network	
Outstrength and Instrength		Outstrength and Instrength	
DDI item	*z*	DDI Item	*z*
Sad	1.02	Done	2.72
Irritable	.99	Concentrate	2.39
Done	.98	Restless	2.16
Enjoy	.94	Effortless	2.03
Concentrate	.88	Sad	1.75
Hopeless	.85	Hopeless	1.56
Worthless	.78	Care	1.53
Tired	.65	Worthless	1.47
Effortless	.63	Irritable	1.41
Restless	.62	Enjoy	1.28
Care	.55	Pace	1.06
Pace	.42	Tired	1.03

Note. z = z-score

In the between-subject network, feeling sad remained the most influential symptom and it significantly related to three symptoms – feeling irritable (*pr* = .31), not enjoying what one was doing (*pr* = .44), and doing things effortfully (*pr* = .40) (Table D.4 in Appendix D). Feeling restless, doing things effortfully, and unable to concentrate significantly correlated with two symptoms. Not enjoying what one was doing, feeling worthless, unable to get things done, and feeling hopeless all significantly related to one symptom. The four symptoms that did not relate to any symptoms were feeling irritable, caring nothing, feeling tired, and not doing thing with one's normal pace. Unable to get things done and unable to concentrate were the most connected nodes in the between-subject network (Table 7.6). The structure of MD was complex, and the symptoms connected differently with other symptoms as seen in the contemporaneous and between-subject networks. One more study was conducted to examine the results of Studies 1 and 2.

Study 3

There were 5,561 data points obtained from 78 participants. The items including "*I have no appetite during the day*", "*I worry about sleeping*", "*I didn't have enough sleep last night*", "*How's your day*" and "*How would you rate your overall physical health today*" were eliminated from mlVAR analysis because they were only measured once a day. There were only 13 significant lagged relationships out of the 169 possible temporal associations and the support for the network theory was rather fragile. Each symptom significantly predicted its' own subsequent symptom ratings (Figure 7.3; Table 7.7). None of the symptoms significantly predicted other symptoms.

The analysis of symptom centrality revealed some symptoms were more important than others. Feeling sad and irritable predicted the most symptoms and feeling guilty and sad were predicted by the most symptoms (Table 7.8). This again weakened the essentialist view because it does not address the relationships between symptoms.

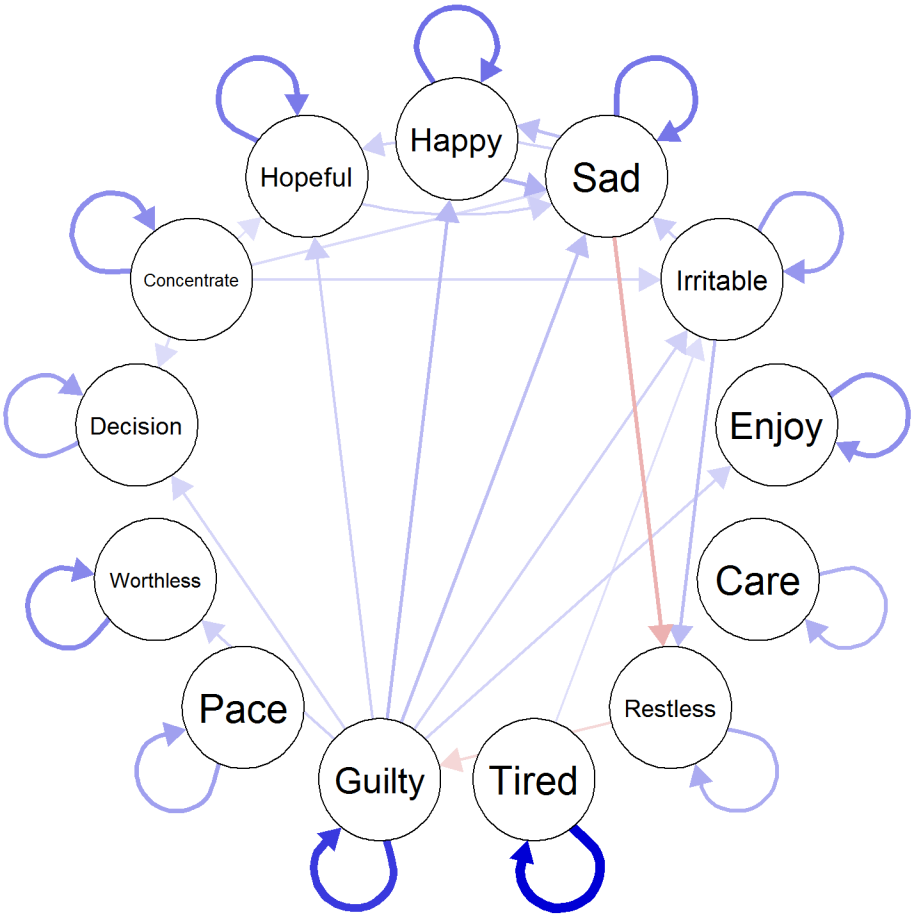


Figure 7.3 Temporal network in Study 3

Table 7.7 *Standardized betas, standard errors, and p-values of the temporal network in Study 3*

From	To	*β*	*SE*	*p*
Happy	Happy	.21	.04	< .001
Happy	Sad	.11	.04	.006
Happy	Irritable	.01	.04	.926
Happy	Enjoy	.08	.04	.185
Happy	Care	-.01	.03	.848
Happy	Restless	.01	.04	.884
Happy	Tired	.00	.04	.977
Happy	Guilty	.02	.03	.645
Happy	Pace	-.01	.04	.926
Happy	Worthless	.02	.03	.645
Happy	Decision	.03	.03	.500
Happy	Concentrate	.02	.03	.692
Happy	Hopeless	.02	.03	.730

From	To	*β*	*SE*	*p*
Sad	Happy	.10	.05	.121
Sad	Sad	.20	.04	< .001
Sad	Irritable	.07	.04	.194
Sad	Enjoy	.03	.04	.602
Sad	Care	.00	.03	.995
Sad	Restless	-.11	.04	.011
Sad	Tired	-.03	.04	.601
Sad	Guilty	.03	.03	.524
Sad	Pace	-.08	.05	.213
Sad	Worthless	.03	.02	.338
Sad	Decision	.04	.03	.396
Sad	Concentrate	.03	.03	.611
Sad	Hopeless	.07	.03	.070
Irritable	Happy	.05	.03	.167
Irritable	Sad	.07	.03	.088
Irritable	Irritable	.15	.04	< .001
Irritable	Enjoy	-.02	.03	.669
Irritable	Care	.03	.02	.318
Irritable	Restless	.10	.03	.006
Irritable	Tired	-.01	.03	.908
Irritable	Guilty	.01	.02	.820
Irritable	Pace	.01	.03	.915
Irritable	Worthless	-.02	.02	.689
Irritable	Decision	.02	.03	.730
Irritable	Concentrate	.05	.03	.223
Irritable	Hopeless	-.01	.02	.719
Enjoy	Happy	.03	.03	.645
Enjoy	Sad	-.04	.02	.255
Enjoy	Irritable	-.01	.04	.894
Enjoy	Enjoy	.16	.03	< .001
Enjoy	Care	-.01	.02	.848
Enjoy	Restless	.02	.03	.684
Enjoy	Tired	.01	.03	.907
Enjoy	Guilty	.03	.02	.427
Enjoy	Pace	.02	.03	.752
Enjoy	Worthless	.01	.02	.745
Enjoy	Decision	.01	.03	.873
Enjoy	Concentrate	-.01	.03	.801
Enjoy	Hopeless	.01	.02	.749
Care	Happy	.03	.05	.768
Care	Sad	.02	.03	.731
Care	Irritable	.06	.04	.315
Care	Enjoy	.00	.04	.957
Care	Care	.12	.03	< .001

From	To	*β*	*SE*	*p*
Care	Restless	-.03	.03	.598
Care	Tired	.00	.03	.943
Care	Guilty	-.01	.04	.849
Care	Pace	.00	.05	.974
Care	Worthless	-.01	.03	.858
Care	Decision	.01	.03	.814
Care	Concentrate	-.02	.03	.731
Care	Hopeless	.01	.02	.873
Restless	Happy	.00	.03	.928
Restless	Sad	.00	.02	.926
Restless	Irritable	.02	.03	.634
Restless	Enjoy	.06	.04	.220
Restless	Care	.01	.02	.919
Restless	Restless	.12	.03	< .001
Restless	Tired	.00	.03	.947
Restless	Guilty	-.06	.02	.029
Restless	Pace	.03	.03	.517
Restless	Worthless	.01	.02	.826
Restless	Decision	-.01	.02	.792
Restless	Concentrate	.02	.03	.753
Restless	Hopeless	-.01	.02	.684
Tired	Happy	-.01	.02	.770
Tired	Sad	.00	.02	.908
Tired	Irritable	.05	.02	.146
Tired	Enjoy	.01	.02	.919
Tired	Care	.01	.02	.721
Tired	Restless	.02	.02	.554
Tired	Tired	.37	.03	< .001
Tired	Guilty	.00	.02	.977
Tired	Pace	.03	.03	.571
Tired	Worthless	-.02	.02	.603
Tired	Decision	.02	.02	.638
Tired	Concentrate	.03	.02	.345
Tired	Hopeless	.00	.02	.974
Guilty	Happy	.10	.03	.011
Guilty	Sad	.10	.03	.011
Guilty	Irritable	.07	.03	.146
Guilty	Enjoy	.07	.03	.142
Guilty	Care	-.01	.03	.777
Guilty	Restless	.06	.04	.261
Guilty	Tired	.00	.04	.957
Guilty	Guilty	.29	.04	< .001
Guilty	Pace	.03	.04	.708
Guilty	Worthless	.07	.03	.082

From	To	*β*	*SE*	*p*
Guilty	Decision	.06	.03	.107
Guilty	Concentrate	.03	.03	.567
Guilty	Hopeless	.07	.03	.025
Pace	Happy	-.03	.03	.417
Pace	Sad	-.02	.02	.663
Pace	Irritable	-.05	.03	.318
Pace	Enjoy	.04	.03	.421
Pace	Care	-.01	.02	.837
Pace	Restless	.00	.02	.947
Pace	Tired	-.01	.03	.826
Pace	Guilty	.00	.02	.926
Pace	Pace	.14	.03	< .001
Pace	Worthless	.00	.02	.919
Pace	Decision	-.01	.03	.764
Pace	Concentrate	.02	.03	.635
Pace	Hopeless	.01	.02	.699
Worthless	Happy	-.02	.04	.796
Worthless	Sad	-.03	.04	.718
Worthless	Irritable	.06	.05	.437
Worthless	Enjoy	.06	.05	.538
Worthless	Care	.05	.06	.622
Worthless	Restless	.02	.05	.784
Worthless	Tired	.05	.05	.538
Worthless	Guilty	.07	.04	.301
Worthless	Pace	.08	.05	.190
Worthless	Worthless	.17	.05	< .001
Worthless	Decision	.01	.04	.947
Worthless	Concentrate	.06	.04	.313
Worthless	Hopeless	-.01	.04	.934
Decision	Happy	.01	.04	.837
Decision	Sad	.05	.03	.334
Decision	Irritable	-.08	.05	.263
Decision	Enjoy	.00	.04	1.000
Decision	Care	.00	.03	.972
Decision	Restless	-.01	.05	.936
Decision	Tired	-.03	.04	.634
Decision	Guilty	.00	.03	.980
Decision	Pace	-.01	.05	.915
Decision	Worthless	.00	.03	1.000
Decision	Decision	.14	.04	< .001
Decision	Concentrate	.05	.03	.321
Decision	Hopeless	.01	.03	.851
Concentrate	Happy	.04	.03	.341
Concentrate	Sad	.06	.03	.134

From	To	*β*	*SE*	*p*
Concentrate	Irritable	.06	.03	.116
Concentrate	Enjoy	.00	.03	.957
Concentrate	Care	.03	.03	.536
Concentrate	Restless	.05	.03	.276
Concentrate	Tired	.05	.03	.292
Concentrate	Guilty	.00	.02	.956
Concentrate	Pace	.04	.03	.420
Concentrate	Worthless	.01	.03	.868
Concentrate	Decision	.05	.02	.116
Concentrate	Concentrate	.17	.04	< .001
Concentrate	Hopeless	.05	.02	.134
Hopeless	Happy	.02	.04	.763
Hopeless	Sad	.07	.03	.121
Hopeless	Irritable	.02	.04	.797
Hopeless	Enjoy	.01	.04	.891
Hopeless	Care	.08	.04	.175
Hopeless	Restless	.04	.05	.622
Hopeless	Tired	.03	.04	.659
Hopeless	Guilty	.02	.03	.715
Hopeless	Pace	.09	.05	.237
Hopeless	Worthless	.05	.03	.336
Hopeless	Decision	-.04	.04	.536
Hopeless	Concentrate	.01	.05	.932
Hopeless	Hopeless	.19	.04	< .001

Note. *β* = standardized beta; *SE* = standard error; *p* = *p*-value.

Table 7.8 *Outstrength and instrength of the nodes in the temporal network in Study 3*

Outstrength		Instrength	
DDI item	*z*	DDI Item	*z*
Sad	.57	Guilty	.68
Irritable	.55	Sad	.62
Restless	.49	Worthless	.50
Happy	.44	Hopeless	.47
Pace	.41	Concentrate	.44
Enjoy	.38	Irritable	.39
Concentrate	.35	Happy	.34
Decision	.30	Decision	.25
Hopeless	.28	Restless	.24
Guilty	.26	Care	.21
Care	.25	Pace	.21
Worthless	.24	Enjoy	.20
Tired	.23	Tired	.19

Note. z = z-score

In the contemporaneous network, unable to concentrate significantly related to four symptoms – not enjoying what one was doing (*pr* = .13), not doing things with one's normal pace (*pr* = .11), unable to make decisions (*pr* = .18), and feeling hopeless (*pr* = .09) (Table D.5 in Appendix D). Feeling happy and feeling irritable significantly associated with three symptoms. Not enjoying what one was doing, feeling restless, feeling guilty, feeling worthless, unable to make decisions, and feeling hopeless related to two symptoms. Feeling sad and caring about nothing only correlated with one symptom. None of the symptoms were related to feeling tired and not doing things with one's normal pace. For centrality analysis, feeling happy and unable to enjoying what one was doing were the best connected DDI items (Table 7.9).

Table 7.9 *Outstrength and instrength of the nodes in the contemporaneous and between-subjects networks in Study 3*

Contemporaneous network		Between-subjects network	
Outstrength and Instrength		Outstrength and Instrength	
DDI item	*z*	DDI Item	*z*
Happy	1.12	Worthless	2.23
Enjoy	.90	Happy	2.14
Concentrate	.89	Hopeless	2.08
Sad	.80	Decision	2.01
Worthless	.80	Irritable	1.87
Irritable	.79	Concentrate	1.71
Hopeless	.77	Restless	1.57
Decision	.75	Enjoy	1.55
Guilty	.63	Guilty	1.52
Restless	.61	Sad	1.47
Care	.56	Tired	1.37
Tired	.48	Pace	.85
Pace	.38	Care	.79

Note. z = z-score

In the between-subject network, feeling happy, feeling irritable, feeling worthless, and unable to concentrate were related to two symptoms (Table D.6 in Appendix D). The symptoms only related to one symptom were feeling sad, not enjoying what one was doing, feeling restless, feeling guilty, unable to make decisions, and feeling hopeless. The three symptoms did not associate with any symptoms were caring nothing, feeling tired, and not doing things with one's own pace. The centrality analysis showed the best-connected symptoms were feeling worthless and feeling happy (Table 7.9). The networks in Study 3 informed the structure of MD is complicated.

Replicability across Studies 1, 2 and 3

Replicability of the networks and centrality was tested by comparing corresponding effect sizes from the three studies using the Spearman's rank-order correlation. To test the replicability of the temporal networks, betas were used, which captured the cross-lagged associations between variables at t and t+1, controlling for all other variables at time t (Epskamp, Waldorp, et al., 2018). Partial-correlation coefficients were employed to test the replicability of the

contemporaneous and between-subject networks, respectively. Before conducting Spearman's rank-order correlation, the DDI items only used in one or two of the studies were removed to align the items across studies. When comparing Studies 1 and 2, not doing things with one's normal pace was eliminated from Study 2. Doing things effortfully and unable to get things done were excluded from Study 2 and feeling happy, feeling guilty, and unable to make decisions were removed from Study 3 before comparing Studies 2 and 3. Prior to comparing Studies 1 and 3, feeling effortless and unable to get things done were eliminated from Study 1 and feeling happy, feeling guilty, and unable to do things according to one's own pace, and unable to make decisions were discarded from Study 3.

For the temporal networks, the betas from Studies 1 and 2, Studies 1 and 3, and Studies 2 and 3 were significantly correlated with each other and the Spearman's rhos were .47, .48, and .48, respectively. The networks were highly replicable because the correlation coefficients were sizeable. For contemporaneous networks, significant associations were found between Studies 1 and 2 and between Studies 2 and 3 and the Spearman's rhos were .60 and .58, respectively. The Spearman's rho of the partial-correlation coefficients between Studies 1 and 3 was .51; however, given that all three correlations were greater than .50, there was likely a degree of replicability beyond what could be expected by chance alone, indicating that residual associations among depression symptoms (controlling for symptoms at previous time-points) did display substantial reliability. Figure 7.4 shows the contemporaneous networks of the three studies side by side.

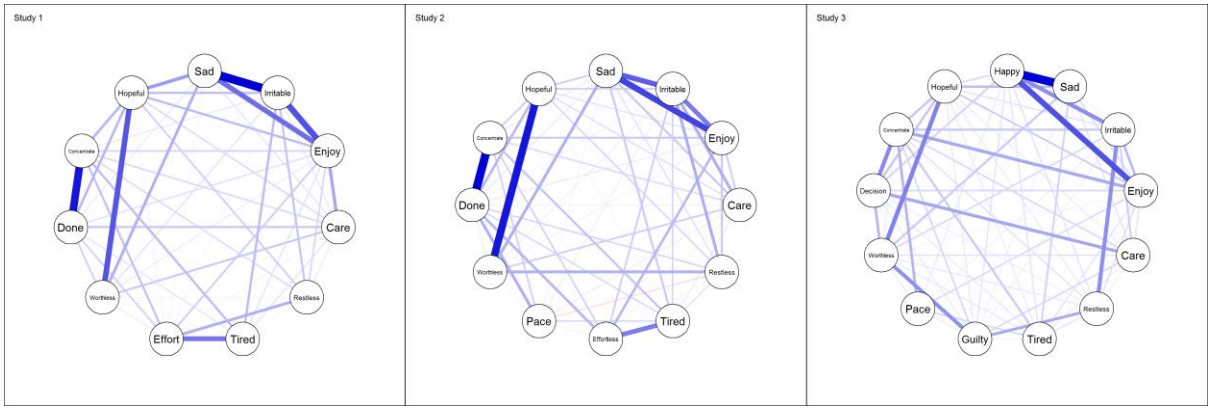


Figure 7.4 The contemporaneous networks in the three studies

The between-subject networks did not replicate. The Spearman's rhos between Studies 1 and 2, between Studies 1 and 3, and between Studies 2 and 3 were .39, .11, and .03, respectively. The between-subject networks of the three studies were shown in Figure 7.5.

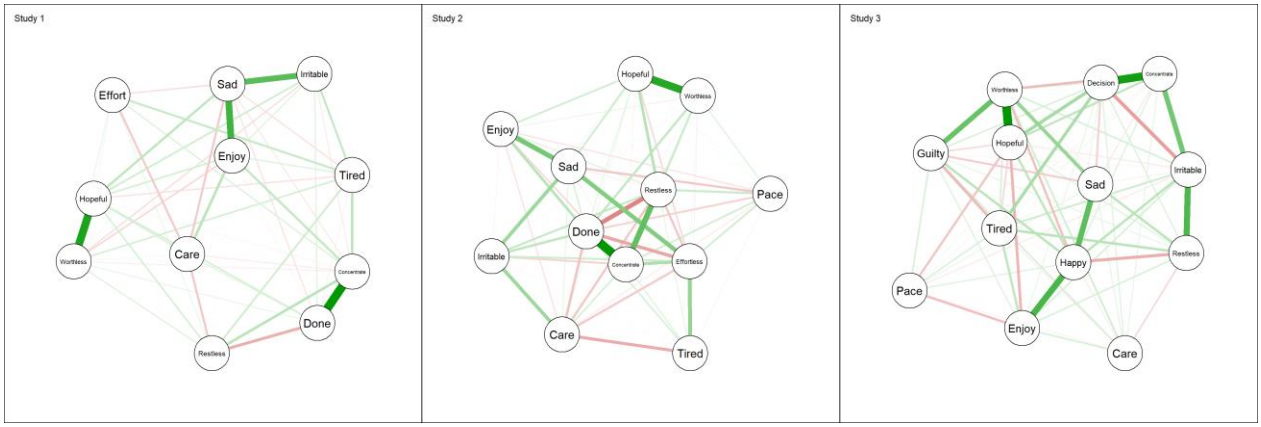


Figure 7.5 The between-subject networks in the three studies

Moderate to great levels of correlation of the Spearman's rhos were found in the instrength of the temporal networks and both outstrength and instrength of the contemporaneous and between-subjects networks (Table 7.10). These sizeable correlations implied considerable replicability in centrality in the two networks.

Table 7.10 *Spearman's rhos of the standardized betas of temporal networks and partial correlation coefficients of contemporaneous and between-subjects networks in Studies 1, 2, and 3*

		r		
		Study 1 vs. Study 2	Study 1 vs. Study3	Study 2 vs. Study 3
Temporal network	Outstrength	-.21	.36	.27
	Instrength	.62	.54	.62
Contemporaneous network	Outstrength and instrength	.85	.64	.78
Between-subjects network	Outstrength and instrength	.23	.33	.32

Note. *r* = Spearman's rho; *p* = *p*-value.

Meta-analysis

Data of 277 participants from three studies were used in a meta-analysis. Only associations shared by the three studies were included in this meta-analysis. Standardized betas and standard errors were used to compute meta-analysis of the temporal networks because it yields reasonably accurate and precise results and the sampling errors are reduced (Peterson & Brown, 2005). For the contemporaneous and between-subject networks, partial correlation coefficients from the three studies were firstly used to calculate standard errors and then the partial correlation coefficients and standard errors were used in the meta-analysis (Figure 7.6).

Similar to the temporal networks in the three studies, there were 14 out of 81 significant associations in the temporal networks across studies (Table 7.11). Thus, rendering some but small support for the network theory. Nonetheless, the standardized betas of the associations were relatively similar and close to zero but most of the large associations were seen in associations between the previous and current measurement of the same symptoms. Unable to concentrate at time t had the most significant associations with other symptoms at time t+1 and these were itself (β = .16), feeling irritable (β = .05), and feeling tired (β = .06). Three significant associations between different symptoms were found – feeling irritable related to feeling sad later (β = .07), feeling worthless now was associated with feeling hopeless later (β = .07), and feeling hopeless was linked to feeling worthless at the next time point (β = .09). These significant associations slightly supported the network theory.

In the contemporaneous and between-subjects networks, there were two and five significant associations, respectively. The two connections in the contemporaneous networks were feeling irritable vs. feeling sad (β = .25) and feeling hopeless vs. feeling worthless (β = .27) (Table 7.12). In the between-subjects networks, the five associations were feeling irritable vs. feeling sad (β = .34), not enjoying what one was doing vs. feeling sad (β = .44), feeling restless vs. feeling

irritable (*β* = .21), unable to concentrate vs. feeling restless (*β* = .25), and feeling hopeless vs. feeling worthless (*β* = .71) (Table 7.13).

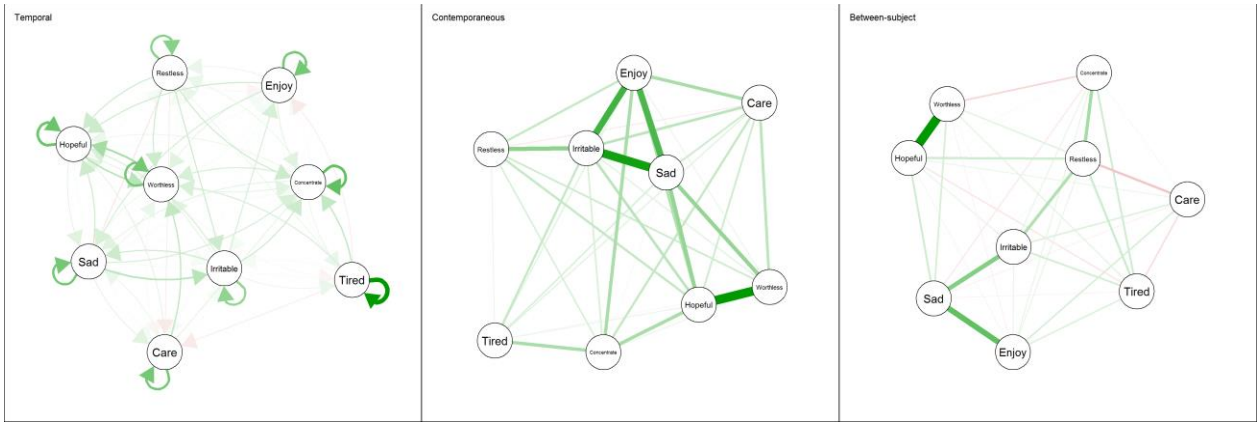


Figure 7.6 Meta-analysis of the temporal, contemporaneous, and between-subject networks in the three studies

Table 7.11 *Meta-analysis of the temporal networks in the three studies* (*N* = 277)

From	To	*β*	*SE*	*z*	*p*
Sad	Sad	.14	.02	7.62	< .001
Sad	Irritable	.05	.02	2.89	.020
Sad	Enjoy	.04	.02	2.31	.082
Sad	Care	.02	.02	.95	.569
Sad	Restless	-.03	.02	-1.43	.344
Sad	Tired	.00	.02	.19	.924
Sad	Worthless	.02	.01	1.87	.183
Sad	Concentrate	.03	.02	1.62	.272
Sad	Hopeless	.03	.01	2.36	.073
Irritable	Sad	.07	.02	3.75	< .001
Irritable	Irritable	.11	.02	5.90	< .001
Irritable	Enjoy	.00	.02	.06	.977
Irritable	Care	.01	.01	.85	.621
Irritable	Restless	.05	.02	2.60	.041
Irritable	Tired	.01	.02	.56	.753
Irritable	Worthless	.00	.01	.17	.926
Irritable	Concentrate	.01	.02	.44	.801
Irritable	Hopeless	.01	.01	.71	.689
Enjoy	Sad	.01	.01	.74	.672
Enjoy	Irritable	.04	.02	2.37	.073
Enjoy	Enjoy	.14	.02	7.40	< .001
Enjoy	Care	.01	.01	1.06	.518
Enjoy	Restless	-.01	.01	-.44	.803

From	To	*β*	*SE*	*z*	*p*
Enjoy	Tired	-.02	.01	-1.14	.474
Enjoy	Worthless	.01	.01	1.13	.477
Enjoy	Concentrate	.01	.01	.50	.777
Enjoy	Hopeless	.01	.01	.97	.557
Care	Sad	.03	.01	1.74	.225
Care	Irritable	.01	.02	.79	.646
Care	Enjoy	.00	.02	.02	.997
Care	Care	.14	.02	8.14	< .001
Care	Restless	-.02	.01	-1.32	.391
Care	Tired	-.02	.01	-1.22	.434
Care	Worthless	-.01	.01	-.54	.762
Care	Concentrate	.00	.01	.01	1.000
Care	Hopeless	.01	.01	1.27	.416
Restless	Sad	.00	.01	-.20	.919
Restless	Irritable	.00	.01	.33	.858
Restless	Enjoy	.02	.02	1.20	.445
Restless	Care	.00	.01	.00	1.000
Restless	Restless	.12	.01	8.31	< .001
Restless	Tired	.02	.01	1.33	.387
Restless	Worthless	.01	.01	.92	.587
Restless	Concentrate	.02	.01	1.44	.340
Restless	Hopeless	.01	.01	.43	.804
Tired	Sad	.01	.01	.95	.569
Tired	Irritable	.02	.01	2.02	.142
Tired	Enjoy	.01	.01	1.07	.513
Tired	Care	.00	.01	.00	1.000
Tired	Restless	.00	.01	.17	.926
Tired	Tired	.26	.01	18.12	< .001
Tired	Worthless	-.01	.01	-.89	.601
Tired	Concentrate	.02	.01	1.31	.399
Tired	Hopeless	.00	.01	.26	.890
Worthless	Sad	.02	.02	1.15	.469
Worthless	Irritable	.03	.02	1.30	.403
Worthless	Enjoy	.03	.02	1.19	.447
Worthless	Care	.06	.02	2.76	.029
Worthless	Restless	.05	.02	2.12	.119
Worthless	Tired	.04	.02	1.62	.269
Worthless	Worthless	.14	.02	6.49	< .001
Worthless	Concentrate	.04	.02	2.29	.085
Worthless	Hopeless	.07	.02	3.99	< .001
Concentrate	Sad	.04	.01	2.43	.063
Concentrate	Irritable	.05	.01	3.69	< .001
Concentrate	Enjoy	.03	.01	2.02	.145
Concentrate	Care	.03	.01	2.03	.142

From	To	*β*	*SE*	*z*	*p*
Concentrate	Restless	.05	.01	3.41	.006
Concentrate	Tired	.06	.01	4.29	< .001
Concentrate	Worthless	.01	.01	1.17	.460
Concentrate	Concentrate	.16	.02	10.49	< .001
Concentrate	Hopeless	.03	.01	2.37	.073
Hopeless	Sad	.05	.02	3.10	.011
Hopeless	Irritable	.04	.02	2.00	.149
Hopeless	Enjoy	.05	.02	2.75	.029
Hopeless	Care	.03	.02	1.38	.366
Hopeless	Restless	.05	.02	2.54	.049
Hopeless	Tired	.00	.02	.01	1.000
Hopeless	Worthless	.09	.02	5.10	< .001
Hopeless	Concentrate	.02	.02	1.02	.536
Hopeless	Hopeless	.15	.02	8.05	< .001

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 7.12 *Meta-analysis of the contemporaneous networks in the three studies* (*N* = 277)

Variable 1	Variable 2	*β*	*SE*	*z*	*p*
Irritable	Sad	.25	.06	4.37	< .001
Enjoy	Sad	.19	.06	3.24	.006
Enjoy	Irritable	.20	.06	3.42	.006
Care	Sad	.05	.06	.83	.633
Care	Irritable	.07	.06	1.16	.465
Care	Enjoy	.09	.06	1.50	.316
Restless	Sad	.01	.06	.17	.926
Restless	Irritable	.12	.06	2.01	.146
Restless	Enjoy	.06	.06	1.02	.536
Restless	Care	-.02	.06	-.38	.831
Tired	Sad	.04	.06	.64	.717
Tired	Irritable	.06	.06	.98	.555
Tired	Enjoy	.03	.06	.49	.780
Tired	Care	.03	.06	.54	.763
Tired	Restless	.02	.06	.27	.889
Worthless	Sad	.11	.06	1.76	.221
Worthless	Irritable	.03	.06	.46	.794
Worthless	Enjoy	.02	.06	.39	.826
Worthless	Care	.07	.06	1.12	.486
Worthless	Restless	.05	.06	.84	.624
Worthless	Tired	.01	.06	.11	.954
Concentrate	Sad	.01	.06	.21	.917
Concentrate	Irritable	.04	.06	.68	.699

Variable 1	Variable 2	*β*	*SE*	*z*	*p*
Concentrate	Enjoy	.09	.06	1.44	.341
Concentrate	Care	.06	.06	.92	.588
Concentrate	Restless	.04	.06	.65	.715
Concentrate	Tired	.09	.06	1.48	.326
Concentrate	Worthless	.02	.06	.25	.892
Hopeless	Sad	.11	.06	1.88	.183
Hopeless	Irritable	.07	.06	1.20	.446
Hopeless	Enjoy	.08	.06	1.26	.420
Hopeless	Care	.05	.06	.76	.667
Hopeless	Restless	.06	.06	.92	.588
Hopeless	Tired	.02	.06	.26	.890
Hopeless	Worthless	.27	.06	4.54	< .001
Hopeless	Concentrate	.09	.06	1.51	.311

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Table 7.13 *Meta-analysis of the between-subjects networks in the three studies* (*N* = 277)

Variable 1	Variable 2	*β*	*SE*	*z*	*p*
Irritable	Sad	.34	.06	6.19	< .001
Enjoy	Sad	.44	.05	8.38	< .001
Enjoy	Irritable	.06	.06	1.05	.522
Care	Sad	-.04	.06	-.66	.713
Care	Irritable	.09	.06	1.53	.306
Care	Enjoy	.11	.06	1.80	.206
Restless	Sad	.03	.06	.54	.764
Restless	Irritable	.21	.06	3.70	< .001
Restless	Enjoy	.06	.06	.94	.577
Restless	Care	-.16	.06	-2.63	.037
Tired	Sad	-.03	.06	-.58	.744
Tired	Irritable	.12	.06	1.96	.157
Tired	Enjoy	.09	.06	1.46	.334
Tired	Care	-.09	.06	-1.58	.285
Tired	Restless	.14	.06	2.26	.091
Worthless	Sad	.11	.06	1.82	.198
Worthless	Irritable	-.02	.06	-.32	.858
Worthless	Enjoy	-.04	.06	-.63	.722
Worthless	Care	.06	.06	1.03	.532
Worthless	Restless	.08	.06	1.33	.387
Worthless	Tired	.07	.06	1.22	.437
Concentrate	Sad	-.06	.06	-.98	.556
Concentrate	Irritable	.06	.06	1.02	.540
Concentrate	Enjoy	.06	.06	1.00	.545

Variable 1	Variable 2	*β*	*SE*	*z*	*p*
Concentrate	Care	.03	.06	.42	.814
Concentrate	Restless	.25	.06	4.38	< .001
Concentrate	Tired	.13	.06	2.19	.107
Concentrate	Worthless	-.11	.06	-1.90	.177
Hopeless	Sad	.13	.06	2.11	.121
Hopeless	Irritable	.06	.06	1.00	.547
Hopeless	Enjoy	.04	.06	.69	.698
Hopeless	Care	.05	.06	.89	.602
Hopeless	Restless	.14	.06	2.40	.067
Hopeless	Tired	-.07	.06	-1.14	.477
Hopeless	Worthless	.71	.04	16.81	< .001
Hopeless	Concentrate	.02	.06	.41	.820

Note. *β* = standardized beta; *SE* = standard error; *z* = *z* score; *p* = *p*-value.

Discussion

The results of the three studies only provided limited and marginal support for the network theory. Excluding auto-correlations, there were only four significant associations out of the 434 possible associations ($p < .001$) (Table 7.14). When the conventional alpha level of .05 was used, the number of significant associations increased to 27 and provided the network theory greater support. The number of significant associations without auto-correlations in meta-analysis was five when the significant level was .001 and it increased to 12 when the alpha level was .05. This provided the network theory with greater support.

Table 7.14 *Total number of associations and the numbers of significant associations (excluding auto-correlations) in the temporal networks in the three studies and meta-analysis*

	Total number of associations	Number of significant associations when $p < .001$	Number of significant associations when $p < .05$
Study 1	121	2	11
Study 2	144	2	8
Study 3	169	0	7
Meta-analysis	81	5	12

The structure of MD was complex as observed in different symptoms taking the leading position in centrality measures of outstrength and instrength in the three networks. There were few significant lagged correlations indicating the existence of unstable and weak causal relationships among some symptoms and thus, vaguely supported the network theory and the MPC view but it did not reject the essentialist view. Also, the temporal networks replicated across the three studies provided the network theory further support. Even though the contemporaneous networks did not fully replicate, the Spearman's rhos were sizeable, there was certain level of replicability. The between-subjects networks did not replicate. The potential issue regarding multiple comparison was taken care of by using false discovery rate to adjust the *p*-values and the adoption of a lower than conventional alpha-level of .001 increased the difficulty to find support for the network theory and made the results more robust (Borsboom et al., 2017; Forbes et al., 2017a, 2017b; Steinley et al., 2017). Nonetheless, MD is a complicated construct so even though the network theory gained some support in this study, it still cannot fully explain MD and other theories are needed to paint a complete picture. Multiple theories are usually necessary to grasp the details of complex constructs such as MD and personality (René Mõttus & Allerhand, 2017). Having the essentialist view together with the network theory in the picture would help us to understand MD in its entirety.

The centrality measures of temporal, contemporaneous, and between-subject networks in the three studies unveiled different MD symptoms were more central than the others in the networks across studies. Variances were observed in symptoms and some symptoms were better connected than others. Slightly consistent with previous research on the connectivity of MD symptoms with other symptoms in temporal networks, where positive affect, hopeless, angry, and irritable were the leading symptoms in generalized anxiety disorder and MD (A. J. Fisher et al., 2017), the weightiest symptom in the three studies was negative affect. They reported the symptoms having the greatest outstrength in contemporaneous networks were feeling down, positive affect, and content. Positive mood had the

greatest outstrength and instrength in the contemporaneous network and the second greatest outstrength and instrength in the between-subjects network in Study 3, which was the only study among the three assessed positive mood. Other symptoms with high outstrength were feeling irritable, feeling sad, and enjoying what one was doing. Poor treatment outcome and severe MD were observed in MD patients who had a high level of anger and hostility (L. B. Fisher et al., 2015). Although none of the correlations in the outstrength and instrength of the three studies and three networks were significant, sizeable replicability was observed in the median to high correlations in the instrength of the temporal networks and the outstrength and instrength of the contemporaneous networks ($r > .5$). The connectivity found in the temporal and contemporaneous networks may support the network theory. However, the symptoms having high outstrength observed in the three studies were different from those reported previously. These discrepancies either enfeeble the replicability of the network theory or suggested centrality rankings diverge greatly among individuals. The latter supports MD as a complex construct and the differences are both in the individual and group level. The fact of varying levels of connectivity among MD symptoms challenged the essentialist view because MD symptoms should not differ in centrality based on the essentialist view.

Overall, the results of the studies in temporal networks and the meta-analytic results (e.g., 14 out of 81 associations had a *p*-value smaller than .001) provided the network theory very limited support. However, the number of significant associations increased when the conventional alpha level was applied. Weighting the pros and cons of adopting a highly conservative alpha level and the possibilities of discovering potential symptom associations are the main deciding factors. When applying network theory in studying psychiatric disorders, one problem in the fundamental assumption was using the DSM (Fried et al., 2017; Guloksuz et al., 2017). The DSM classification system have been revised several times since the publication of its first edition. As mentioned in Chapter 1 of this thesis, the most recent version – the DSM-V – received a huge amount of criticism.

This inevitably affected relevant scientific research, pharmacological studies, and clinical trainings and practices. Bearing these drawbacks in mind, the potential contributions or insights of the network theory might bring to psychiatry cannot be undermined. As the theory gathered more and more interests from various parties, the advancement and improvement of the theory may inspire professionals working in the field of psychiatry to see mental disorders from various perspectives.

Limitations and future directions

The recording frequency of data limits the changes in symptoms that could be pinned down in networks (Epskamp, van Borkulo, et al., 2018). Future studies may test different frequencies of data collection to capture the most obvious temporal changes in MD symptoms or utilize big data recorded every second to map out the microscopic and meaningful fluctuations and associations among symptoms (Kitchin, 2014).

Chapter 8 General discussion: MD is a heterogeneous construct

"The mind is attracted to ideas that refer to effects with single causes, possess a broad application and are concordant with contemporary ethical premises. However, most psychological phenomena are not the product of a single cause, the concepts that account for a relation between two measurements are usually limited in breath, and the current emphasis on biological contributions to behaviors and symptoms is a pleasing idea because it promises the certainty associated with materialistic causes and is in accord with the relatively recent ethical imperative to avoid blaming the victim…" (Kagan, 2007, p. 372)

There are three types of heterogeneity in major depression (MD): signs, symptoms, and syndromes, etiology, and dimensional heterogeneity – blending of normal and clinical symptoms (Monroe & Anderson, 2015). Here we discuss the heterogeneity in MD symptoms (Chapters 1–7) and the heterogeneity in the etiology of MD (Chapter 7).

The debate surrounding whether MD is homogeneous or heterogeneous was mentioned in Chapter 1. According to the Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V), the diagnosis of MD is established when five or more of the nine MD symptoms are present within two weeks (American Psychiatric Association, 2013b). Among the five or more MD symptoms, at least one must be either depressed mood or anhedonia. Taking a closer look of the MD symptoms, some symptoms comprise opposite descriptions such as insomnia vs. hypersomnia. In addition, the sum-score scheme has been challenged by research reporting variances observed in MD symptoms such as impairments in psychosocial functioning and the underlying biological mechanisms, how they were affected by life events, and how they comorbid with other disorders, and their relationships

with personality traits, MD episodes, and demographics (Fried & Nesse, 2014; Fried et al., 2014; Lux & Kendler, 2010).

Summary of findings and contributions and relevance within the literature

Across the seven chapters, heterogeneity in MD symptoms is a shared observation. It could be observed in the inter-correlations between MD symptoms in Chapter 2, the associations between MD symptom variability and MD severity and moderators in Chapter 3, the relationships between MD symptoms and circadian rhythm in Chapter 4, the relationships between MD symptoms and personality traits and facets in Chapter 5, the relationships between MD symptoms and activity level and heart rate variability in Chapter 6, and the temporal relationships between MD symptoms in Chapter 7. The details of the findings from each chapter were described below.

In Chapter 2, heterogeneity of MD symptoms was found in inter-correlations between the very first momentary MD ratings participants responded. Comparing the inter-correlations between the mean momentary MD ratings and between retrospective MD ratings showed the mean momentary MD ratings were highly inter-correlated and this may be explained by they were the stable estimates of MD symptoms because they were the averages. Further testing of the inter-correlations between the very first retrospective MD ratings revealed symptom variabilities as seen in the weak inter-correlations across the three studies and the large ranges of PCA loadings.

In Chapter 3, MD symptom heterogeneity was observed in the relationships between the variabilities of MD symptoms and MD severity as measured by the Patient Health Quality-9 (PHQ-9) in the three studies and a meta-analysis of the three studies. None or only a few of the variabilities in MD symptoms were significantly predicted by moderators including age, gender, educational attainment, employment status, and marital status. However, within-subject variabilities, the standard deviations of the momentary MD ratings, were moderately inter-

correlated as indicated by the variances explained by the first principal components in the three studies and the correlations between PCA loadings. But the ranges of PCA loadings in the three studies reflected a certain degree of variance between symptom variabilities.

In Chapter 4, only some MD symptoms were significantly predicted by the afternoon and evening measuring times in the three studies and meta-analysis. The varying predictability of measuring times on MD symptoms might suggest MD symptoms are heterogeneous.

In Chapter 5, significant associations were only observed between some personality traits and facets and some of the PHQ-9 and the Daily Depressive Items (DDI). In addition, broad ranges of standardized betas obtained from meta-analyses of personality traits and the PHQ-9 items, the means of the DDI items, and the standard deviations of the DDI items were observed. These were between the PHQ-9 items and neuroticism and extraversion, between the means of the DDI items and neuroticism, extraversion, and conscientiousness, and between the standard deviations of the DDI items and neuroticism and conscientiousness.

In Chapter 6, there were sparing significant associations between activity level and heart rate variability and within- and between-subject differences.

In Chapter 7, when using a stringent alpha level of .001 on top of false discovery rate to correct for multiple comparisons, marginal support for the network theory were found in the temporal networks in the three studies and meta-analysis. While using the conventional alpha level (and still controlling for multiple testing) provided the network theory with more support. Also, different MD symptoms were found to occupy varying positions in the symptom network, having different levels of centrality in the temporal, contemporaneous, and between-subject

networks and thereby showing the varying importance of symptoms, which is in line with previous research on MD symptoms.

Heterogeneity in MD symptoms challenges the current diagnostic criteria

These observations of heterogeneity in MD symptoms may place the diagnostic criteria currently in use in a questionable position because it uses sum scores in clinical diagnoses. The unspoken presumptions of adopting sum scores and cut-offs to establish boundaries between nonclinical and clinical populations might be "all symptoms are interchangeable and equally good indicators" (Fried & Nesse, 2015b, p. 72) or "the same weight is given to each item" (van Eeden et al., 2019, p. 203). However, neglecting the variances between patients' expressions of symptoms – having varying combinations of symptoms – and differences in individual symptoms and treating them as a whole may take its toll on the general population including both the clinical and nonclinical population. Even more, the resources spend on relevant research.

Nomothetic versus idiographic view

Nomothetic view of using a large sample is widely adopted in psychological research while idiographic view of investigating intraindividual differences is gradually gaining more attention. Despite many might believe the nomothetic approach could be used to deduce general laws that apply to every individual, it actually informs "the distribution of variables at the level of the population through the use of summary statistics … and help to determine what applied to the *aggregate* – that is, when averaging across individuals … What applies in *aggregate* is not necessarily informative on what is true in *general*" (Hamaker, 2012, p. 2). Ergodicity discusses the conditions when between-subject analysis yields the same results in individuals. Two requirements have to be meet to apply results obtained from between-subject analyses to each individual – individuals in both the sampling population and the population the results would be applied to are homogenous and the phenomenon under study is stable or "have constant statistical characteristics in time" (P. C. Molenaar & Campbell, 2009, p. 115). Differences between between- and within-subject differences have been reported. The results of between-subject

analysis were found to be substantially different from those of within-subject analysis – the idiosyncratic view (A. J. Fisher et al., 2017; Hamaker, 2012; Laukka et al., 2018; van Eeden et al., 2019). Conducting within-subject research requires a considerable amount of repeated measurements from the same individual, which might be hard to collect in the past due to the availability of suitable tools. But the progressions in mobile and computing technologies have made data collection and analysis easier than before (A. J. Fisher et al., 2017; Hamaker, 2012).

This thesis also investigates the divergences between intraindividual and interindividual differences and the repeated measure data collected in the three studies via the adoption of experience sampling methodology to investigate the differences between the two approaches.

In Chapter 6, there were no differences between within- and between-subject differences in low physical activity level and MD symptoms. The associations between low heart rate variability and MD symptoms were only found in within-subject differences. Between- and within-subject differences in activity level and heart rate activity exhibited varying patterns. Replicability of within-individual differences was not tested in Chapter 6 because activity level and heart rate variability data were collected in one of the three studies.

In Chapter 7, to compare the structures of within- and between-subject networks, the correlations of the meta-analytic networks were analyzed. The correlations between the networks were sizeable in magnitude. The correlations of temporal vs. contemporaneous (r = .31), temporal vs. between-subject networks (r = .38), and contemporaneous vs. between-subject networks (r = .59) were moderate in magnitude: collectively for three correlations to exceed .3 is unlikely by chance, however the between- and within-subject networks were thus generally moderately similar.

The within-individual differences networks did replicated in Chapter 7. The associations between the temporal networks from the three studies were

moderately correlated. Sizeable associations were found between the contemporaneous networks ($r > .5$). Replicability of within-individual differences was not tested in Chapter 6 because only one study was included in this chapter.

Limitations

While the results of this thesis to some degree challenge the assumption of MD symptoms being homogeneous and support heterogeneity in MD symptoms, there are several limitations in the materials and participants.

The participants in the three studies were mostly healthy undergraduate students in the University of Edinburgh. Their responses to both the retrospective and momentary questionnaires might differ from the clinical population even though some of the participants had a PhQ-9 score that exceeded the cut-off of MD diagnosis of 10. However, examining the number of participants with a PHQ-9 score equal to or greater than the cut-off found the participants in this thesis well represented a matching population of undergraduate students. In Studies 1, 2, and 3, 62 out of 124, 23 out of 75, and 24 out of 78 participants had a PHQ-9 score of 10 or greater, respectively (Table 8.1). In a review of 24 articles, the prevalence of MD was 10% – 85% and a weighted mean prevalence is 30.6% (Ibrahim et al., 2013). This shows the participants in the three studies were representative of their age group. The prevalence of MD in the general population is 10.4% in 12 months and 20.6% over a lifetime in the U.S. (Hasin et al., 2018). The relatively high prevalence might indicate the mental health of undergraduate students should be taken more seriously and handy supports might need to be placed for them. In addition, the participants shared similar demographics including age, educational attainment, employment status, and marital status, which may make the effects of these variables undistinguishable.

Extracting the data of the participants whose PHQ-9 score equal to or greater than the cut-off might yield more informative findings of the clinical population than analyzing the data of all participants collectively.

Table 8.1 *The distribution of PHQ-9 scores in Studies 1, 2, and 3*

PHQ-9 score	Study 1	Study 2	Study 3
0	5	1	4
1	8	4	1
2	7	7	14
3	8	4	6
4	5	7	8
5	9	7	2
6	6	8	2
7	5	7	5
8	4	3	6
9	5	4	6
10	4	4	5
11	8	0	2
12	15	4	4
13	4	1	2
14	4	2	1
15	4	3	2
16	3	4	2
17	2	0	0
18	5	3	1
19	4	1	0
20	1	0	0
21	3	0	1
22	0	0	1
23	1	0	1
24	1	0	1
25	1	0	1
26	1	0	0
27	1	1	0
Prevalence	50%	30.67%	30.77%

Note. Prevalence shows the percentage of participants with a PHQ-9 score equal to or greater than 10.

The materials used in the three studies were on-line and mobile questionnaires and activity sensors. Since every material and method has its pros, cons, and limitations, so do the materials and methods employed in this thesis. To paint a full picture of a complex construct such as MD, applying multiple methods would speed up the process of putting the puzzles together as suggested by Georg von Bekesy, a Nobel laureate, to an early career researcher (as cited in Kagan, 2007).

One of the premises of adopting the single-symptom approach in studying MD is whether the measurements are reliable. The convergent and divergent validity of the DDI was tested in Chapter 2, where the DDI items measuring the same symptoms showed greater convergence than those measuring different symptoms. However, there were only one to three DDI items dedicated to measure individual MD symptom, which places the reliability of these measurements in a dangerous position (Fried & Nesse, 2015b). Having several questions measuring each symptom might increase the reliability of the measurements.

Several MD symptoms comprise opposite sub-symptoms and these include insomnia and hypersomnia, weight gain and weight loss, appetite gain and appetite loss, and psychomotor retardation and psychomotor agitation. In this thesis, these sub-symptoms were not extracted and were analyzed collectively. For example, participants' ratings on "I have no appetite during the day" ranged from "Have appetite" to "Don't have appetite" on a 100-point sliding scale. Participants' ratings for this question could be separated into below and above 50 and analyzed separately to investigate the implications on a sub-symptom level.

Implications and possible applications

Since depressive symptoms are different and heterogeneous and there might be network-like relationships among them, constructing networks to find out the relationships between the depressive symptoms in each patient might help the clinicians to identify vital symptoms in patients. Clinicians could then focus on treating these symptoms to prevent other symptoms from emerging. Practically, this could be done firstly by following the patients for several weeks or months. Later, the data could be used to construct temporal and contemporaneous networks of the depressive symptoms. Once the key symptoms were identified, the clinicians could then tailor treatment plans to alleviate the key symptoms. During the course of the treatment, the clinicians could also observe the efficacy of the treatment plans and make adjustments when needed. For example, if feeling tired is a key symptom, monitoring the fatigue level and sending notifications to remind the patient to take a nap or walk whenever his/her fatigue level raises to an

alarming level may prevent other symptoms from occurring. This may ultimately make a depressive episode to stop at an early stage or reduce the severity of an episode. This could be pictured as removing a few dominos from a chain of dominos in an ongoing domino show to stop the chain reaction.

The MD symptoms being dissimilar rather than similar as reflected in their associations with several variables may have challenged the diagnostic criteria of MD listed in the two mainstream classification systems because the depressive symptoms were treated as if they all have equal weight in diagnoses. Therefore, the results of this thesis might provide some insights to re-examine the diagnostic criteria of MD. This echoed different initiatives of developing new classification systems - the RDoC project sponsored by the NIH (Insel, 2013) and the HiTOP model (Kotov et al., 2017).

Future directions

Some of the data collected in the three studies were not analyzed but they might provide some insights to MD research. These include lifestyle questions, quality of the closest relationship, and three open questions – "Do these questions reflect depressive symptoms? Why?", "In your opinion, could these questions be refined to detect finer changes? How? Can you give some examples?", and "In general, what are other suggestions you have toward this study?" Looking into the implications of lifestyle questions and the quality of the closest relationship might show the influences of these factors on MD symptoms. Analyzing the open questions would bring in a qualitative aspect and it might provide some fresh inputs from the participants.

Another possibly interesting aspect might be to change the initial retrospective questions in the PHQ-SADS into predictive questions and ask the participants to predict their feelings over the period of data collection to explore the relationship between predictions and symptom severity.

Collecting ESM data from MD patients might yield results closer to the real experiences of patients suffering from the disorder. However, the MD prevalence in the three groups of participants did corresponded with the MD prevalence in the

similar age group in the general population, extracting the data of those participants whose PHQ-9 score equal to or greater than 10 might provide informative predictive results of an age-matched patient group.

The results from clinical population could obtain applicable results that are beneficial to improve and develop clinical treatments and applications. In addition, the data could be used to compare the differences, similarities, and overlaps between the non-clinical and clinical population. These could be used to formulate a broad symptom spectrum across the two population.

Adopting objective measures such as symptom checklists or asking family members or friends of the participants to rate the MD symptoms they observed in the participants may yield more accurate measures of MD. It could balance the biases in self-reports because they are pertain to biases (Furnham et al., 2016; Rosenman et al., 2011). After such adjustment, a decrease in the prevalence of MD and greater symptom heterogeneity might be observed in the three groups of participants. This would coincide the varied symptom profiles in MD patients as reported in Fried and Nesse (2015a).

Conclusions

The overall conclusion of this thesis is MD symptoms are heterogeneous, therefore, they should not be treated collectively and the usage of sum-total score in clinical diagnoses should be reconsidered for the furtherance of relevant fields and the welfare of those who are affected by MD. Investigating within-individual differences might bring forth invaluable fruits in progressing what we think we know about MD and shine more light on diagnosis, treatment, and research.

Appendix A: Questionnaires used in the three studies

Demographic and lifestyle questions used in Studies 1 and 2

1. What is your gender?

Male Female

2. How old are you? _____

3. What is your highest level of education? (Or the closest equivalent)

A. Primary

B. GCSE

C. A level/Highers

D. Bachelor's degree

E. Master's Degree

F. PhD

4. What's your marital status?

A. Single

B. Married

C. Divorced

D. Widowed

E. In a relationship

5. What's your employment status?

A. Employed or self-employed

B. Part-time employed

C. Full-time student

D. Retired

E. Unemployed

6. Where do you find the information about this study?

A. Invitation email from the researcher

B. Social media (e.g., Facebook)

C. Invitation email from the Hope Park Counselling Centre

D. Approached by the researcher

E. School email

F. Poster

G. Other

7. Which of the following statement best describes your usual diet?

A. Fresh veg, meat, fish, and dairy products.

B. No meat.

C. 4-6 times of frozen or pre-made meals a week

D. Mainly snacks

E. Only veggie

F. Special medical diet

8. Do you smoke?

A. No

B. Less than 1 cigarette a day

C. 1-9 cigarettes a day

D. 11-20 cigarettes a day

E. More than 21 cigarettes a day

9. Do you drink alcohol?

A. No

B. Once in a while

C. 1-2 glasses of wine or 0.5-1 pint of beer a day

D. 3-6 glasses of wine or 1.5-3 pints of beer a day

E. More than 7 glasses of wine or 3.5 pints of beer a day

10. Have you been diagnosed, treated, medicated, or monitored for any of the following?
Asthma, metabolic syndrome (i.e., heart disease, stroke, diabetes), frequent colds, arthritis, or other major medical conditions.

A. No

B. I recovered.

C. I am receiving treatment.

D. I am waiting for the diagnosis.

11. How often do you exercise for more than 30 minutes?

A. Daily

B. 2-4 times a week

C. Once a week

D. Once a month

E. Seldom

F. I cannot exercise because of physical problems.

Note. One item was added in Study 3 - "What's the quality of your closest relationship?". It has two anchoring points of "very good" and "very poor" on a 9-point Likert scale.

Table A.1 *PHQ-SADS*

Please answer every question to the best of your ability.
A. During the last 4 weeks, how much have you been bothered by any of the following problems?

	Not bothered	Bothered a little	Bothered a lot
Stomach pain			
Back pain			
Pain in your arms, legs, or joints (knees, hips, etc.)			
Feeling tired or having little energy			
Trouble falling or staying asleep, or sleeping too much			
Menstrual cramps or other problems with your periods			
Pain or problems during sexual intercourse			
Headaches			
Chest pain			
Dizziness			
Fainting spells			
Feeling your heart pound or race			
Shortness of breath			
Constipation, loose bowels, or diarrhea			
Nausea, gas, or indigestion			

B. Over the last 2 weeks, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
Feeling nervous anxiety or on the edge				
Not being able to stop or control worrying				
Worrying too much about different things				
Trouble relaxing				
Being so restless that it is hard to sit still				
Becoming easily annoyed or irritable				
Feeling afraid as if something awful might happen				

C. Questions about anxiety attacks

	Yes	No
In the last 4 weeks, have you had an anxiety attack - suddenly feeling fear or panic?		
Has this ever happened before?		
Do some of these attacks come suddenly out of the blue - that is, in situations where you don't expect to be nervous or uncomfortable?		
Do these attacks bother you a lot or are you worried about having another attack?		
During your last bad anxiety attack, did you have symptoms like shortness of breath, sweating, or your heart racing pounding or skipping?		

D. Over the last 2 weeks, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
Little interest or pleasure in doing things				
Feeling down, depressed, or hopeless				
Trouble falling or staying asleep, or sleeping too much				
Feeling tired or having little energy				
Poor appetite or overeating				
Feeling bad about yourself - or that you are a failure or have let yourself or your family down				
Trouble concentrating on things, such as reading the newspaper or watching television				
Moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual				
Thoughts that you would be better off dead of or hurting yourself in some way				

E. If you checked off any problems on this questionnaire (PHQ-SADS), how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?
Not difficult at all
Somewhat difficult
Very difficult
Extremely difficult

Table A.2 *IPIP*

The following statements concern your perception about yourself in a variety of situations. Your task is to indicate the strength of your agreement with each statement, choosing the best response on the scale ranging from strong disagreement (1) to strong agreement (7). There is no right" or "wrong" answers, so select the responses that most closely reflect you in general. Take your time and consider each statement carefully. Answering all the questions can take between 15 and 20 minutes.

	Item	Anchoring points and response scale						
		Strongly Disagree						Strongly Agree
		1	2	3	4	5	6	7
1	I worry about things							
2	I fear for the worst							
3	I am afraid of many things							
4	I often feel blue							
5	I get stressed out easily							
6	I get angry easily							
7	I get irritated easily							
8	I lose my temper							
9	I am not easily annoyed							
10	I dislike myself							
11	I am often down in the dumps							
12	I feel comfortable with myself							
13	I find it difficult to approach others							
14	I am afraid to draw attention to myself							
15	I only feel comfortable with friends							
16	I am not bothered by difficult social situations							
17	I go on binges							
18	I rarely overindulge							
19	I easily resist temptations							
20	I am able to control my cravings							
21	I panic easily							
22	I become overwhelmed by events							
23	I feel that I'm unable to deal with things							
24	I remain calm under pressure							
25	I make friends easily							
26	I feel comfortable around people							
27	I avoid contacts with others							
28	I prefer to be alone							
29	I keep others at a distance							

	Item	Anchoring points and response scale
30	I love large parties	
31	I talk to a lot of different people at parties	
32	I avoid crowds	
33	I take charge	
34	I try to lead others	
35	I take control of things	
36	I wait for others to lead the way	
37	I am always busy	
38	I am always on the go	
39	I do a lot in my spare time	
40	I like to take it easy	
41	I love excitement	
42	I seek adventure	
43	I enjoy being reckless	
44	I act wild and crazy	
45	I radiate joy	
46	I have a lot of fun	
47	I love life	
48	I look at the bright side of life	
49	I have a vivid imagination	
50	I enjoy wild flights of fantasy	
51	I love to daydream	
52	I like to get lost in thought	
53	I believe in the importance of art	
54	I see beauty in things that others might not notice	
55	I do not like poetry	
56	I do not enjoy going to art museums	
57	I experience my emotions intensely	
58	I feel others' emotions	
59	I rarely notice my emotional reactions	
60	I don't understand people who get emotional	
61	I prefer variety to routine	
62	I prefer to stick with things that I know	
63	I dislike changes	
64	I am attached to conventional ways	
65	I love to read challenging material	
66	I avoid philosophical discussions	
67	I have difficulty understanding abstract ideas	
68	I am not interested in theoretical discussions	
69	I tend to vote for liberal political candidates	
70	I believe that there is no absolute right and wrong	
71	I tend to vote for conservative political candidates	

	Item	Anchoring points and response scale
72	I believe that we should be tough on crime	
73	I trust others	
74	I believe that others have good intentions	
75	I trust what people say	
76	I distrust people	
77	I use others for my own ends	
78	I cheat to get ahead	
79	I take advantage of others	
80	I obstruct others' plans	
81	I am concerned about others	
82	I love to help others	
83	I am indifferent to the feelings of others	
84	I take no time for others	
85	I love a good fight	
86	I yell at people	
87	I insult people	
88	I get back at others	
89	I believe that I am better than others	
90	I think highly of myself	
91	I have a high opinion of myself	
92	I boast about my virtues	
93	I sympathize with the homeless	
94	I feel sympathy for those who are worse off than myself	
95	I am not interested in other people's problems	
96	I try not to think about the needy	
97	I complete tasks successfully	
98	I excel in what I do	
99	I handle tasks smoothly	
100	I know how to get things done	
101	I like to tidy up	
102	I often forget to put things back in their proper place	
103	I leave a mess in my room	
104	I leave my belongings around	
105	I keep my promises	
106	I tell the truth	
107	I break rules	
108	I break my promises	
109	I do more than what's expected of me	
110	I work hard	
111	I put little time and effort into my work	
112	I do just enough work to get by	
113	I am always prepared	
114	I carry out my plans	

	Item	Anchoring points and response scale
115	I waste my time	
116	I have difficulty starting tasks	
117	I jump into things without thinking	
118	I make rash decisions	
119	I rush into things	
120	I act without thinking	

Table A.3 *Daily Depression Items used in Study 1*

How do you feel right now of the following?

	Items	Anchoring points and response scale	
		0	100
1	I feel sad.	Happy	Sad
2	I feel irritable.	Cheerful	Irritable
3	I enjoy what I am doing.	Enjoy	Don't enjoy
4	I don't care about anything.	Care	Don't care
5	I had no appetite during the day.**	Have appetite	Don't have appetite
6	I worry about sleeping.**,***	Worry about sleeping	Don't worry about sleeping
7	I feel that I didn't have enough sleep last night.*	Enough sleep	Not enough sleep
8	I am restless.***	Restless	Not restless
9	I am tired.	Not tired	Tired
10	It is not effortful to do things.***	Effortful	Effortless
11	I feel worthless.	Not worthless	Worthless
12	I feel that I can't get anything done.	Getting things done	Not getting things done
13	I can't concentrate.	Can concentrate	Cannot concentrate
14	I feel hopeless.***	Hopeless	Hopeful
15	How's your day?**	Very good	Not very good

Note. * Items only presented in the first sampling time of the day; ** Items only presented at the last sampling time of the day; *** Reverse scoring items. This questionnaire was designed based on the DSM-V diagnostic criteria: depressed mood, Items 1 and 2; loss of interest or pleasure, Items 3 and 4; altered appetite, Item 5; sleep disturbance, Items 6 and 7; psychomotor changes, Items 8 and 10; decreased energy, tiredness, or fatigue, Item 9; sense of worthlessness, Items 11 and 12; impaired ability to think, concentrate, or make decisions, Item 13; thoughts of death, suicidal ideation, and suicidal attempts, Item 14.

Table A.4 *Daily Depression Items used in Study 2*

How do you feel right now of the following?

	Items	Anchoring points		
		0		100
1	I feel sad.	Happy		Sad
2	I feel irritable.	Calm		Irritable
3	I enjoy what I am doing.	Enjoy		Don't enjoy
4	I don't care about anything.	Care		Don't care
5	I have no appetite during the day.**	Have appetite		Don't have appetite
6	I worry about sleeping.**, ***	Worry about sleeping		Don't worry about sleeping
7	I feel that I didn't have enough sleep last night.*	Enough sleep		Not enough sleep
8	I am restless.***	Restless		Not restless
9	I am tired.	Not tired		Tired
10	It is not effortful to do things.	Effortless		Effortful
11	I am doing things with my normal pace.	Faster	Normal	Slower
12	I feel worthless.***	Worthless		Not worthless
13	I feel that I can't get anything done.	Getting things done		Not getting things done
14	I can't concentrate.	Can concentrate		Cannot concentrate
15	I feel hopeless.***	Hopeless		Hopeful
16	How's your day?**	Very good		Not very good
17	How would you rate your overall physical health today?**	Very good		Not very good

Note. * Items only presented in the first sampling time of the day; ** Items only presented at the last sampling time of the day; *** Reverse scoring items. This questionnaire was designed based on the DSM V diagnostic criteria: depressed mood, Items 1 and 2; loss of interest or pleasure, Items 3 and 4; altered appetite, Item 5; sleep disturbance, Items 6 and 7; psychomotor changes, Items 8, 10, and 11; decreased energy, tiredness, or fatigue, Item 9; sense of worthlessness, Items 12 and 13; impaired ability to think, concentrate, or make decisions, Item 14; thoughts of death, suicidal ideation, and suicidal attempts, Item 15.

Table A.5 *Daily Depression Items used in Study 3*

How do you feel right now of the following?

	Items	Anchoring points		
		0		100
1	What time did you go to bed last night?*			
2	What time did you wake up this morning?*			
3	I feel happy.***	Not at all		Very much
4	I feel sad.	Not at all		Very much
5	I feel irritable.	Calm		Irritable
6	I enjoy what I am doing.	Enjoy		Don't enjoy
7	I don't care about anything.	Care		Don't care
8	I have no appetite during the day.**	Have appetite		Don't have appetite
9	I worry about sleeping.**, ***	Worry about sleeping		Don't worry about sleeping
10	I didn't have enough sleep last night.*	Enough sleep		Not enough sleep
11	I am restless.***	Restless		Not restless
12	I am tired.	Not tired		Tired
13	I feel guilty.***	Guilty		Not guilty
14	I am doing things at my normal pace.	Faster	Normal	Slower
15	I feel worthless.***	Worthless		Not worthless
16	I feel that I can't make decisions.	Can make decisions		Cannot make decisions
17	I can't concentrate.	Can concentrate		Cannot concentrate
18	I feel hopeless.***	Hopeless		Hopeful
19	How's your day?**	Very good		Not very good
20	How would you rate your overall physical health today?**	Very good		Not very good

Note. * Items only presented at the first sampling time of a sampling day; ** Items only presented at the last sampling time of a sampling day; *** Reverse scoring items. This questionnaire was designed based on the DSM-V diagnostic criteria: depressed mood, Items 3 – 5; loss of interest or pleasure, Items 6 and 7; altered appetite, Item 8; sleep disturbance, Items 9 and 10; psychomotor changes, Items 11 and 14; decreased energy, tiredness, or fatigue, Item 12; sense of worthlessness, Items 13 and 15; impaired ability to think, concentrate, or make decisions, Items 16 and 17; thoughts of death, suicidal ideation, and suicidal attempts, Item 18.

Table A.6 *Mapping of the DDI items across the three studies*

	Study 1	Study 2	Study 3
1. I feel happy.			x
2. I feel sad.	x	x	x
3. I feel irritable.	x	x	x
4. I enjoy what I am doing.	x	x	x
5. I don't care about anything.	x	x	x
6. I have no appetite during the day.	x	x	x
7. I worry about sleeping.	x	x	x
8. I feel that I don't have enough sleep last night.	x	x	x
9. I am restless.	x	x	x
10. I am tired.	x	x	x
11. It is not effortful to do things.	x	x	
12. I feel guilty.			x
13. I am doing things at my normal pace.		x	x
14. I feel worthless.	x	x	x
15. I feel that I can't get anything done.	x	x	
16. I feel that I can't make decisions.			x
17. I can't concentrate.	x	x	x
18. I feel hopeless.	x	x	x
19. How's your day?	x	x	x
20. How would you rate your overall physical health today?		x	x

Note. x = this item is used.

Appendix B: R codes of the models in the chapters

Chapter 3

lm(scale(the SD of the each of DDI items) ~ scale(PHQ-9 score) + scale(Age) + scale(Education) + Gender + Marital status + Employment status)

Chapter 4

Model 1 = lmer(scale(the momentary measures of each of the DDI items) ~ scale(PHQ-9 score) + scale(Age) + scale(Education) + Gender + Marital status + Employment status + time + (1|ID))

Model 2 = lmer(scale(the momentary measures of each of the DDI items) ~ scale(PHQ-9 score) + scale(Age) + scale(Education) + Gender + Marital status + Employment status + time + (1 + time|ID))

Model 3 = lmer(scale(the momentary measures of each of the DDI items) ~ scale(PHQ-9 score) * time + scale(Age) + scale(Education) + Gender + Marital status + Employment status + (1|ID))

Chapter 5

lm(scale(the score of each of the PHQ-9 item/the means of each of the DDI items/the SD of each of the DDI items) ~ scale(each personality trait and facet) + scale(Age) +scale(Education) + Gender + Marital status + Employment status)

Chapter 6

lmer(scale(the means of activity levels) ~ scale(the momentary measures of each of the DDI items) + scale(Age) + scale(Education) + Gender + Marital status + Employment status + (1|ID))

The activity levels were aggregates of acceleration measured 30, 60, and 120 minutes before and after the momentary measures of the DDI items.

Appendix C

Figure C.1 Standardized betas of PHQ-9 score from regression models in Studies 1, 2, and 3

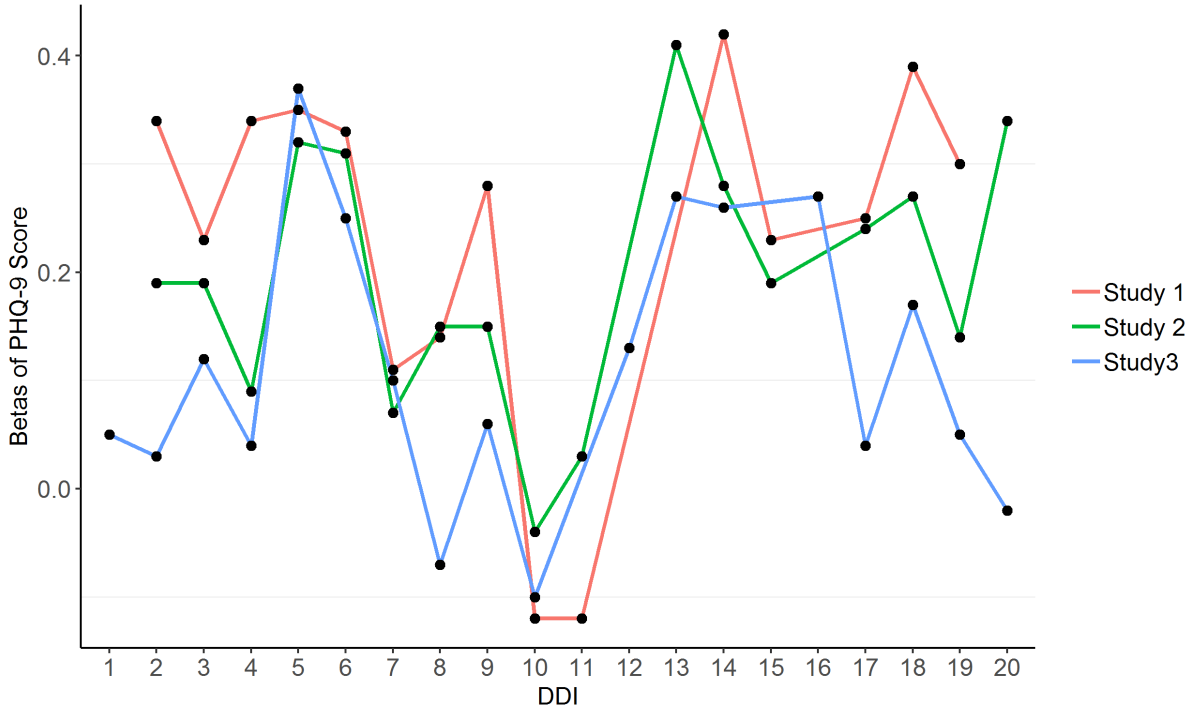


Figure C.2 Standardized betas of age from regression models in Studies 1, 2, and 3

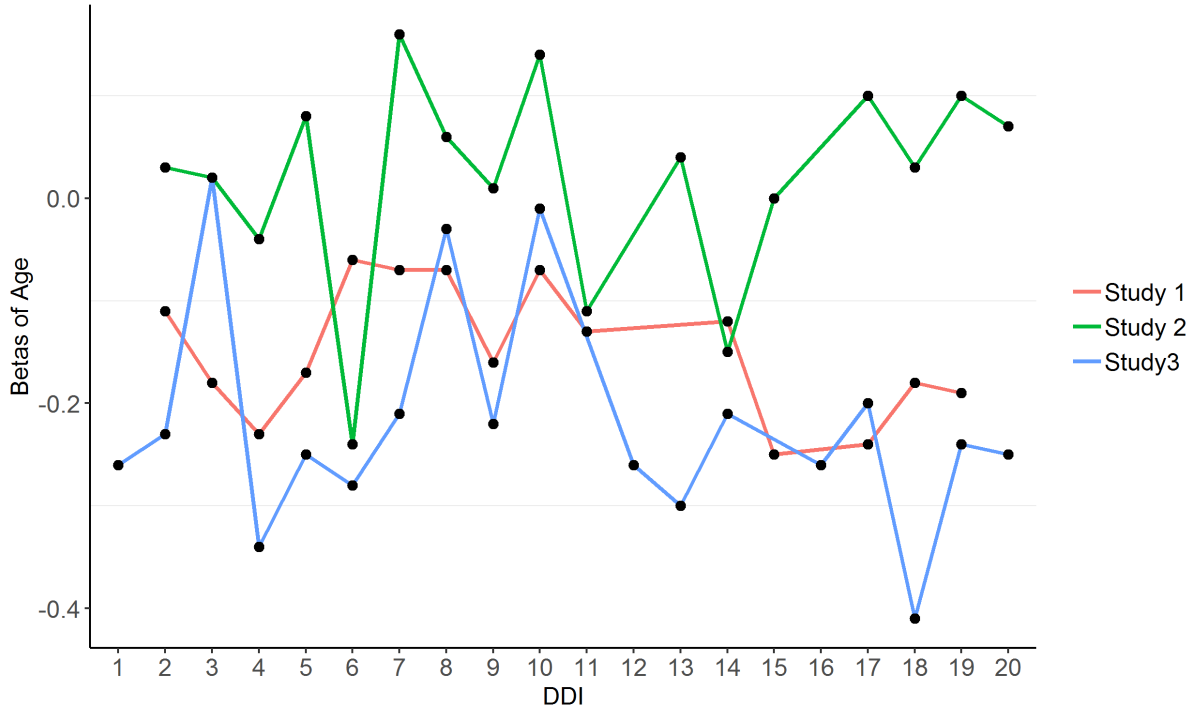


Figure C.3 Standardized betas of gender from regression models in Studies 1, 2, and 3

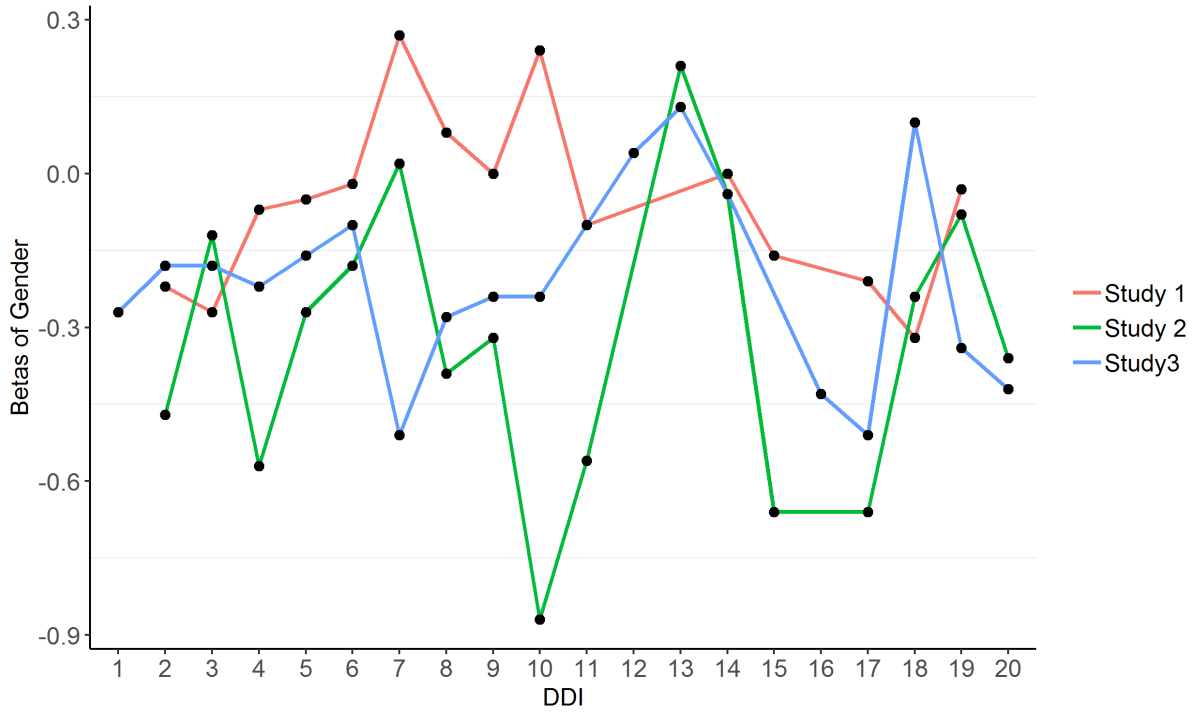


Figure C.4 Standardized betas of educational attainment from regression models in Studies 1, 2, and 3

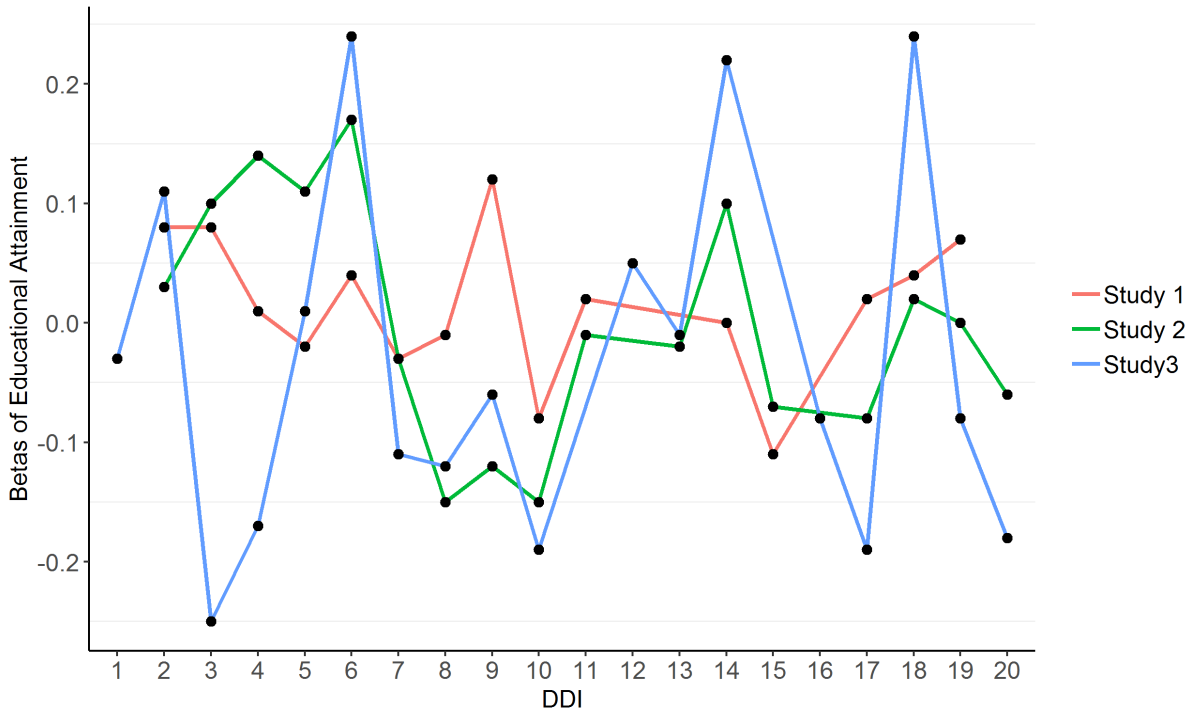


Figure C.5 Standardized betas of marital status from regression models in Studies 1, 2, and 3

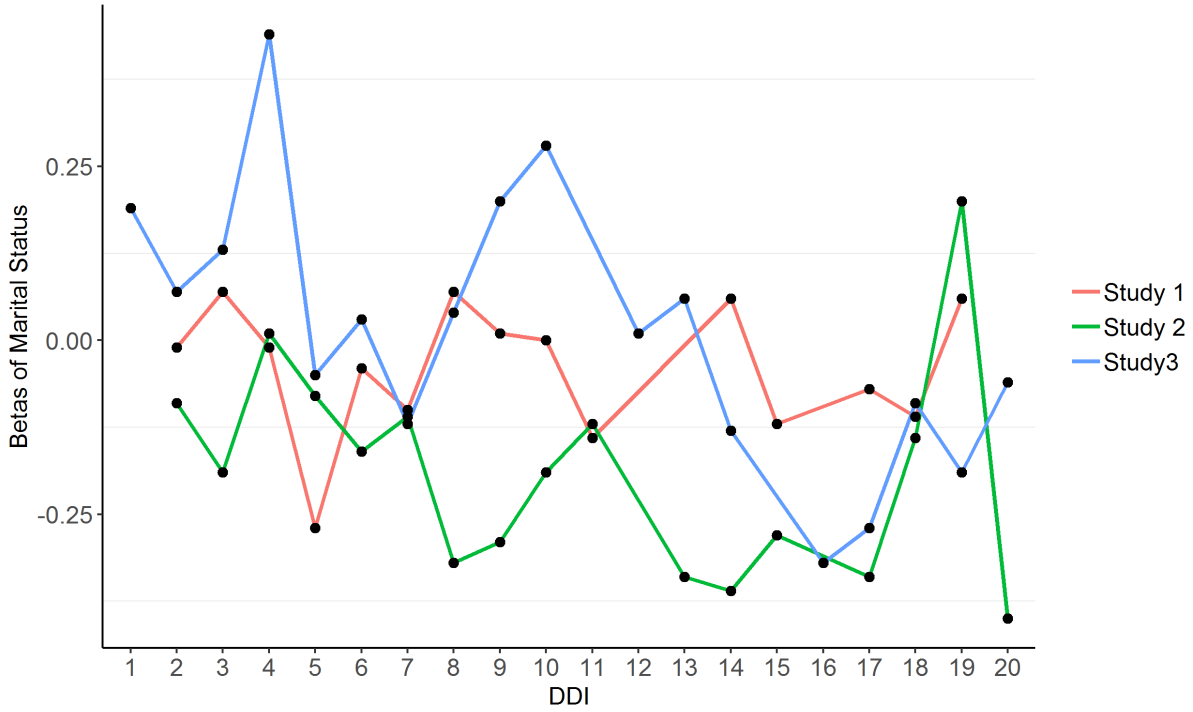
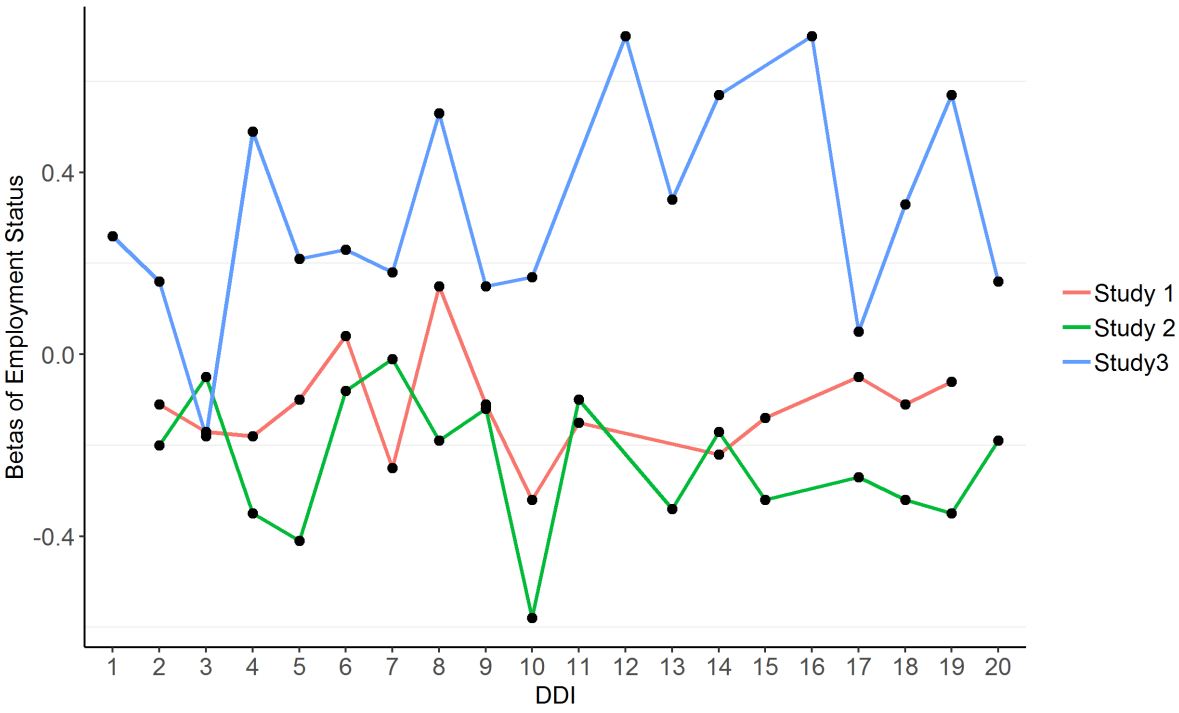


Figure C.6 Standardized betas of employment status from regression models in Studies 1, 2, and 3



Appendix D

Table D.1 *Partial correlation coefficients and p-values of the contemporaneous network in Study 1*

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Irritable	Sad	.38	< .001	< .001
Enjoy	Sad	.22	< .001	< .001
Enjoy	Irritable	.26	< .001	< .001
Care	Sad	.04	.267	.045
Care	Irritable	.03	.116	.455
Care	Enjoy	.13	< .001	< .001
Restless	Sad	-.01	.474	.932
Restless	Irritable	.09	< .001	< .001
Restless	Enjoy	.06	.011	.011
Restless	Care	-.04	.213	.338
Tired	Sad	.00	.984	.797
Tired	Irritable	.10	< .001	< .001
Tired	Enjoy	.04	.041	.073
Tired	Care	.04	.119	.110
Tired	Restless	-.01	.638	.903
Effort	Sad	.01	.699	.550
Effort	Irritable	.01	.570	.699
Effort	Enjoy	.07	< .001	< .001
Effort	Care	-.02	.426	.471
Effort	Restless	.12	< .001	< .001
Effort	Tired	.20	< .001	< .001
Worthless	Sad	.12	< .001	< .001
Worthless	Irritable	.04	.226	.126
Worthless	Enjoy	.03	.270	.239
Worthless	Care	.08	< .001	< .001
Worthless	Restless	.02	.669	.416
Worthless	Tired	-.01	.680	.633
Worthless	Effort	.03	.340	.162
Done	Sad	.03	.263	.192
Done	Irritable	.01	.496	.831
Done	Enjoy	.05	.091	.112
Done	Care	.08	< .001	< .001
Done	Restless	-.01	.748	.831
Done	Tired	.04	.175	.105
Done	Effort	.06	.006	< .001
Done	Worthless	.07	.011	< .001
Concentrate	Sad	.00	.853	.974

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Concentrate	Irritable	.03	.381	.079
Concentrate	Enjoy	.06	< .001	< .001
Concentrate	Care	.06	.016	.006
Concentrate	Restless	.05	.016	.052
Concentrate	Tired	.10	< .001	< .001
Concentrate	Effort	.09	< .001	< .001
Concentrate	Worthless	.01	.629	.764
Concentrate	Done	.35	< .001	< .001
Hopeful	Sad	.15	< .001	< .001
Hopeful	Irritable	.09	< .001	< .001
Hopeful	Enjoy	.10	< .001	< .001
Hopeful	Care	.05	.033	.006
Hopeful	Restless	.07	< .001	< .001
Hopeful	Tired	.01	.770	.912
Hopeful	Effort	.02	.338	.501
Hopeful	Worthless	.25	< .001	< .001
Hopeful	Done	.11	< .001	< .001
Hopeful	Concentrate	.11	< .001	< .001

Note. v1 = variable 1; v2 = variable 2; *p* = *p*-value

Table D.2 *Partial correlation coefficients and p-values of the between-subjects network in Study 1*

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Irritable	Sad	.53	< .001	< .001
Enjoy	Sad	.61	< .001	< .001
Enjoy	Irritable	.09	.414	.681
Care	Sad	-.17	.185	.170
Care	Irritable	.01	.932	.837
Care	Enjoy	.22	.153	< .001
Restless	Sad	-.02	.691	.738
Restless	Irritable	.01	.784	.794
Restless	Enjoy	.01	.973	.947
Restless	Care	-.18	.116	.160
Tired	Sad	-.09	.366	.853
Tired	Irritable	.19	.162	.079
Tired	Enjoy	.10	.416	.730
Tired	Care	-.01	.926	.804
Tired	Restless	.14	.107	.555
Effort	Sad	-.10	.460	.517
Effort	Irritable	-.04	.869	.636

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Effort	Enjoy	.01	.946	.729
Effort	Care	-.16	.115	.237
Effort	Restless	.06	.794	.595
Effort	Tired	.17	.200	.107
Worthless	Sad	.04	.842	.780
Worthless	Irritable	-.10	.321	.628
Worthless	Enjoy	-.12	.198	.689
Worthless	Care	.04	.808	.738
Worthless	Restless	.10	.378	.579
Worthless	Tired	.13	.185	.461
Worthless	Effort	.06	1.000	.391
Done	Sad	-.08	.474	.784
Done	Irritable	.09	.545	.602
Done	Enjoy	-.03	.928	.782
Done	Care	.09	.400	.645
Done	Restless	-.26	.020	.016
Done	Tired	-.05	.769	.784
Done	Effort	.00	.823	.889
Done	Worthless	.07	.604	.698
Concentrate	Sad	-.07	.836	.418
Concentrate	Irritable	-.06	.712	.668
Concentrate	Enjoy	.19	.156	.129
Concentrate	Care	-.06	.545	.869
Concentrate	Restless	.22	.045	.070
Concentrate	Tired	.21	.115	.059
Concentrate	Effort	.10	.301	.616
Concentrate	Worthless	-.05	.868	.617
Concentrate	Done	.83	< .001	< .001
Hopeful	Sad	.20	.101	.088
Hopeful	Irritable	.14	.098	.731
Hopeful	Enjoy	.13	.126	.837
Hopeful	Care	.12	.091	.753
Hopeful	Restless	.13	.363	.272
Hopeful	Tired	-.09	.416	.689
Hopeful	Effort	.05	.448	.974
Hopeful	Worthless	.73	< .001	< .001
Hopeful	Done	.13	.364	.311
Hopeful	Concentrate	-.03	.805	.540

Note. v1 = variable 1; v2 = variable 2; *p* = *p*-value

Table D.3 *Partial correlation coefficients and p-values of the contemporaneous network in Study 2*

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Irritable	Sad	.25	< .001	< .001
Enjoy	Sad	.29	< .001	< .001
Enjoy	Irritable	.20	< .001	< .001
Care	Sad	.08	.020	.006
Care	Irritable	.12	< .001	< .001
Care	Enjoy	.08	.011	.029
Restless	Sad	.05	.237	.110
Restless	Irritable	.13	< .001	< .001
Restless	Enjoy	.08	.006	.006
Restless	Care	.00	.974	.995
Tired	Sad	.08	< .001	< .001
Tired	Irritable	.06	.016	.020
Tired	Enjoy	.00	.972	.919
Tired	Care	.03	.261	.431
Tired	Restless	.04	.228	.363
Effortless	Sad	-.01	.846	.968
Effortless	Irritable	.07	.006	.016
Effortless	Enjoy	.11	< .001	< .001
Effortless	Care	-.02	.632	.797
Effortless	Restless	-.02	.700	.607
Effortless	Tired	.20	< .001	< .001
Pace	Sad	.02	.874	.381
Pace	Irritable	-.03	.616	.295
Pace	Enjoy	.01	.669	1.000
Pace	Care	-.03	.678	.262
Pace	Restless	-.05	.150	.292
Pace	Tired	.06	.283	.020
Pace	Effortless	.02	.718	.496
Worthless	Sad	.12	< .001	< .001
Worthless	Irritable	-.03	.435	.601
Worthless	Enjoy	.02	.497	.556
Worthless	Care	.07	.016	.049
Worthless	Restless	.12	< .001	< .001
Worthless	Tired	.01	.730	.897
Worthless	Effortless	.01	.919	.731
Worthless	Pace	.01	.675	.894
Done	Sad	.03	.309	.349
Done	Irritable	.02	.768	.487
Done	Enjoy	.03	.369	.423
Done	Care	.02	.569	.581
Done	Restless	.06	.056	.121

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Done	Tired	.06	.098	.146
Done	Effortless	.11	< .001	< .001
Done	Pace	.12	< .001	< .001
Done	Worthless	.03	.444	.698
Concentrate	Sad	.03	.465	.416
Concentrate	Irritable	.01	.744	.738
Concentrate	Enjoy	.08	< .001	.033
Concentrate	Care	.05	.206	.011
Concentrate	Restless	.01	.718	.943
Concentrate	Tired	.09	.006	< .001
Concentrate	Effortless	.06	.041	.020
Concentrate	Pace	.07	.029	.049
Concentrate	Worthless	.01	.774	.765
Concentrate	Done	.39	< .001	< .001
Hopeful	Sad	.07	.025	.052
Hopeful	Irritable	.07	.020	.011
Hopeful	Enjoy	.04	.294	.262
Hopeful	Care	.05	.366	.025
Hopeful	Restless	.06	.041	.059
Hopeful	Tired	.02	.873	.486
Hopeful	Effortless	-.01	.919	.846
Hopeful	Pace	.00	.869	.951
Hopeful	Worthless	.36	< .001	< .001
Hopeful	Done	.11	< .001	< .001
Hopeful	Concentrate	.07	.006	.037

Note. v1 = variable 1; v2 = variable 2; *p* = *p*-value

Table D.4 *Partial correlation coefficients and p-values of the between-subjects network in Study 2*

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Irritable	Sad	.31	.029	< .001
Enjoy	Sad	.44	< .001	< .001
Enjoy	Irritable	-.03	.616	.919
Care	Sad	.07	.960	.240
Care	Irritable	.31	.041	< .001
Care	Enjoy	-.08	.793	.399
Restless	Sad	-.05	.926	.701
Restless	Irritable	.18	.461	.119
Restless	Enjoy	.09	.612	.646
Restless	Care	-.17	.377	.190

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Tired	Sad	-.01	.846	.943
Tired	Irritable	-.02	.858	.699
Tired	Enjoy	-.02	.554	.391
Tired	Care	-.27	.037	.037
Tired	Restless	.07	.759	.677
Effortless	Sad	.40	< .001	< .001
Effortless	Irritable	.15	.436	.202
Effortless	Enjoy	-.01	.977	.926
Effortless	Care	-.16	.480	.146
Effortless	Restless	-.18	.157	.361
Effortless	Tired	.34	< .001	.011
Pace	Sad	-.18	.056	.520
Pace	Irritable	-.01	.591	.620
Pace	Enjoy	-.08	.699	.545
Pace	Care	-.06	.645	.858
Pace	Restless	.16	.196	.416
Pace	Tired	.04	.908	.716
Pace	Effortless	.13	.157	.640
Worthless	Sad	.02	.699	.833
Worthless	Irritable	-.02	.782	.988
Worthless	Enjoy	.06	.974	.545
Worthless	Care	.04	.638	.973
Worthless	Restless	.16	.506	.190
Worthless	Tired	-.05	.919	.694
Worthless	Effortless	-.03	.997	.777
Worthless	Pace	.09	.405	.730
Done	Sad	.11	.759	.361
Done	Irritable	.20	.150	.241
Done	Enjoy	.22	.292	.063
Done	Care	-.19	.607	.070
Done	Restless	-.39	.011	< .001
Done	Tired	.13	.311	.607
Done	Effortless	-.28	.112	.006
Done	Pace	-.14	.556	.278
Done	Worthless	.18	.200	.295
Concentrate	Sad	-.04	.780	.436
Concentrate	Irritable	-.14	.544	.295
Concentrate	Enjoy	-.12	.223	.737
Concentrate	Care	.13	.548	.367
Concentrate	Restless	.50	< .001	< .001
Concentrate	Tired	.09	.638	.602
Concentrate	Effortless	.26	.177	.011
Concentrate	Pace	.13	.276	.499

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Concentrate	Worthless	-.14	.270	.569
Concentrate	Done	.81	< .001	< .001
Hopeful	Sad	.15	.602	.177
Hopeful	Irritable	.05	.784	.826
Hopeful	Enjoy	.15	.262	.474
Hopeful	Care	.05	.889	.731
Hopeful	Restless	.23	.067	.211
Hopeful	Tired	.00	.836	.837
Hopeful	Effortless	-.11	.292	.751
Hopeful	Pace	.03	.978	.777
Hopeful	Worthless	.69	< .001	< .001
Hopeful	Done	.07	.837	.555
Hopeful	Concentrate	-.04	.957	.730

Note. v1 = variable 1; v2 = variable 2; *p* = *p*-value

Table D.5 *Partial correlation coefficients and p-values of the contemporaneous network in Study 3*

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Sad	Happy	.39	< .001	< .001
Irritable	Happy	.17	< .001	< .001
Irritable	Sad	.02	.498	.733
Enjoy	Happy	.26	< .001	< .001
Enjoy	Sad	.05	.150	.253
Enjoy	Irritable	.11	.006	< .001
Care	Happy	-.01	.770	.911
Care	Sad	.04	.292	.490
Care	Irritable	.08	.006	.025
Care	Enjoy	.04	.149	.384
Restless	Happy	.04	.445	.137
Restless	Sad	.01	.869	.919
Restless	Irritable	.17	< .001	< .001
Restless	Enjoy	.05	.167	.194
Restless	Care	-.03	.641	.569
Tired	Happy	.04	.496	.324
Tired	Sad	.07	.016	.052
Tired	Irritable	-.01	.886	.718
Tired	Enjoy	.04	.298	.272
Tired	Care	.03	.366	.428
Tired	Restless	.04	.380	.504
Guilty	Happy	.04	.196	.240

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Guilty	Sad	.02	.715	.547
Guilty	Irritable	-.03	.604	.689
Guilty	Enjoy	.01	.614	.941
Guilty	Care	.06	.237	.085
Guilty	Restless	.13	< .001	< .001
Guilty	Tired	.02	.638	.681
Pace	Happy	.03	.369	.426
Pace	Sad	.00	.794	.696
Pace	Irritable	-.02	.689	.421
Pace	Enjoy	.05	.239	.076
Pace	Care	.01	.932	.700
Pace	Restless	.01	.777	.722
Pace	Tired	.06	.134	.110
Pace	Guilty	.03	.730	.474
Worthless	Happy	.00	.926	.768
Worthless	Sad	.08	.041	.016
Worthless	Irritable	.06	.177	.056
Worthless	Enjoy	.02	.763	.669
Worthless	Care	.05	.344	.270
Worthless	Restless	.04	.167	.590
Worthless	Tired	.04	.221	.571
Worthless	Guilty	.17	< .001	< .001
Worthless	Pace	.03	.379	.671
Decision	Happy	.07	.011	.056
Decision	Sad	-.01	.802	.479
Decision	Irritable	.00	.890	.865
Decision	Enjoy	.06	.126	.150
Decision	Care	.13	< .001	< .001
Decision	Restless	.02	.659	.405
Decision	Tired	.04	.255	.438
Decision	Guilty	.03	.594	.433
Decision	Pace	.02	.926	.584
Decision	Worthless	.11	.016	.029
Concentrate	Happy	-.01	.952	.662
Concentrate	Sad	.01	.678	.782
Concentrate	Irritable	.08	.076	.033
Concentrate	Enjoy	.13	< .001	< .001
Concentrate	Care	.06	.206	.052
Concentrate	Restless	.05	.194	.267
Concentrate	Tired	.08	.011	.011
Concentrate	Guilty	.06	.165	.067
Concentrate	Pace	.11	< .001	.006
Concentrate	Worthless	.03	.731	.439

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Concentrate	Decision	.18	< .001	< .001
Hopeful	Happy	.06	.280	.112
Hopeful	Sad	.10	< .001	.011
Hopeful	Irritable	.04	.157	.369
Hopeful	Enjoy	.08	.011	.033
Hopeful	Care	.03	.493	.602
Hopeful	Restless	.03	.558	.423
Hopeful	Tired	.03	.700	.226
Hopeful	Guilty	.03	.642	.421
Hopeful	Pace	.00	.903	.908
Hopeful	Worthless	.19	< .001	< .001
Hopeful	Decision	.09	.033	.059
Hopeful	Concentrate	.09	.020	< .001

Note. v1 = variable 1; v2 = variable 2; *p* = *p*-value

Table D.6 *Partial correlation coefficients and p-values of the between-subjects network in Study 3*

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Sad	Happy	.45	< .001	< .001
Irritable	Happy	.19	.037	.468
Irritable	Sad	-.04	.869	.770
Enjoy	Happy	.51	< .001	< .001
Enjoy	Sad	.01	.782	.890
Enjoy	Irritable	.11	.794	.248
Care	Happy	.00	.730	.530
Care	Sad	.07	.248	.782
Care	Irritable	-.01	.456	.419
Care	Enjoy	.10	.426	.593
Restless	Happy	-.22	.029	.217
Restless	Sad	.19	.088	.291
Restless	Irritable	.49	< .001	< .001
Restless	Enjoy	.10	.662	.448
Restless	Care	-.11	.291	.567
Tired	Happy	-.03	1.000	.738
Tired	Sad	.03	.730	1.000
Tired	Irritable	.13	.949	.020
Tired	Enjoy	.17	.263	.307
Tired	Care	-.05	.754	.746
Tired	Restless	.19	.270	.116
Guilty	Happy	.19	.126	.261
Guilty	Sad	-.14	.366	.301

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Guilty	Irritable	-.02	.634	.820
Guilty	Enjoy	.08	.513	.820
Guilty	Care	.11	.388	.419
Guilty	Restless	.06	.987	.376
Guilty	Tired	-.19	.404	.037
Pace	Happy	.08	.794	.369
Pace	Sad	.05	.748	.759
Pace	Irritable	-.06	.421	.974
Pace	Enjoy	-.18	.183	.206
Pace	Care	-.03	.770	.884
Pace	Restless	-.01	.987	.950
Pace	Tired	.10	.380	.707
Pace	Guilty	.10	.241	.753
Worthless	Happy	-.17	.140	.372
Worthless	Sad	.29	.033	.016
Worthless	Irritable	.11	.712	.358
Worthless	Enjoy	.00	.907	.919
Worthless	Care	.12	.410	.369
Worthless	Restless	-.03	.908	.823
Worthless	Tired	.10	.784	.378
Worthless	Guilty	.42	< .001	< .001
Worthless	Pace	.02	.331	.620
Decision	Happy	.05	.794	.782
Decision	Sad	-.13	.730	.221
Decision	Irritable	-.26	.045	.020
Decision	Enjoy	.06	.664	.889
Decision	Care	.08	.622	.642
Decision	Restless	.09	.586	.640
Decision	Tired	.24	.016	.307
Decision	Guilty	.10	.975	.228
Decision	Pace	.03	.426	.789
Decision	Worthless	.07	.283	.803
Concentrate	Happy	.09	.669	.604
Concentrate	Sad	-.06	.629	.823
Concentrate	Irritable	.39	< .001	< .001
Concentrate	Enjoy	.02	.952	.928
Concentrate	Care	.06	.879	.595
Concentrate	Restless	-.01	.543	.744
Concentrate	Tired	.04	.846	.623
Concentrate	Guilty	.00	.946	.973
Concentrate	Pace	-.03	.789	.919
Concentrate	Worthless	-.19	.132	.338
Concentrate	Decision	.66	< .001	< .001

v1	v2	Partial correlation coefficient	*p* (v1 to v2)	*p* (v2 to v1)
Hopeful	Happy	.18	.642	.020
Hopeful	Sad	-.02	.974	.765
Hopeful	Irritable	-.06	.879	.592
Hopeful	Enjoy	-.20	.734	.006
Hopeful	Care	-.05	.671	.823
Hopeful	Restless	.08	.679	.614
Hopeful	Tired	-.10	.237	.858
Hopeful	Guilty	-.10	.327	.768
Hopeful	Pace	-.16	.568	.076
Hopeful	Worthless	.71	< .001	< .001
Hopeful	Decision	.25	.073	.056
Hopeful	Concentrate	.17	.283	.297

Note. v1 = variable 1; v2 = variable 2; *p* = *p*-value

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